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Table of Contents.

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Page.

ORIGINAL ARTICLES—
The Prothrombin Test in Clinical Medicine, by E. R. Trethewie and P. A. Melvin 189
Streptomycin in Tuberculosis, by J. Bell Ferguson, V. G. Bristow and P. R. Bull 192
Industrial Dermatitis, by Edward Rosanove, M.R.C.P., M.R.A.C.P. 194
The Nature, Recognition and Treatment of Glaucoma, by Arthur D'Ombrain, M.B., Ch.M., D.O.M.S., F.R.A.C.S. (Oph.) 196
A Brief Review of Industrial Dermatoses in Western Australia, by J. M. O'Donnell 200
Non-Eczematous Industrial Dermatitis, by J. Summons 202
Recent Experiences in London on the Use of Physical Medicine in Arthritis, by John A. Shanasy 203
Streptomycin in Pulmonary Tuberculosis: A Review of Six Cases, by R. Munro Ford 205
The Royal Prince Alfred Hospital Cancer of the Uterus Follow-Up, by Herbert H. Schlink, Clement L. Chapman and Frederick N. Chenhall 206

REPORTS OF CASES—
Morbilli Bullosi, by S. E. J. Robertson, M.B., B.S., M.R.A.C.P. 208
Chronic Nephritis in a Child of Twelve, by Geoffrey Serpell 209

REVIEWS—
Gastro-Enterology 210
Hearing and its Preservation 210
Drugs from Plants 211
Hæmolytic Phenomena 211
A Year Book of Dermatology and Syphilology .. 211
A Text-Book of Anæsthetics 211
Humanism as a Philosophy 212

Page.

BOOKS RECEIVED 212

LEADING ARTICLES—
New Operations for the Relief of Mitral Stenosis 213

CURRENT COMMENT—
Streptomycin and Chronic Bone Infections 214
Protein Comes into its Own 215

ABSTRACTS FROM MEDICAL LITERATURE—
Pædiatrics 216
Orthopædic Surgery 216

SPECIAL ARTICLE—
The Diagnosis of Poliomyelitis 218

BRITISH MEDICAL ASSOCIATION NEWS—
Scientific 220

CORRESPONDENCE—
Control of Hyperthyreoidism by Propyl Thiouracil: A Clinical Inquiry 222
Blood Alcohol Content: Some Aspects of its Post-Mortem Uses 223

DISEASES NOTIFIABLE IN EACH STATE AND TERRITORY OF AUSTRALIA 223

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—
Queensland 224
New South Wales 224

DIARY FOR THE MONTH 224

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 224

EDITORIAL NOTICES 224

THE PROTHROMBIN TEST IN CLINICAL MEDICINE.

By E. R. TRETHEWIE AND P. A. MELVIN,

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Owing to the increase in the use of dicoumarol in the therapy of patients suffering from various thrombotic conditions, the performance of the prothrombin test has increased greatly. It is also being used as a test for hepatic efficiency.[16] For example, at this Institute in the past year 1149 tests were performed in the routine department. There have been a number of different techniques described for carrying out this test, but in this paper a plea is made for the test as carried out on the lines laid down by Quick in 1940.[9] Quick[10] later produced evidence that prothrombin is composed of a labile component A and a stable component B. In experiments to determine an essential cause for the development of thrombosis in the hind limb, perfusions were carried out on the hind limbs and pelvis of the cat. It was found that the perfused fluid was more coagulable than the control, and when the graph time from the prothrombin graph was read, it was found that this indicated that there was a rise in the "prothrombin" content. Since it was recognized that this indicated a rise in prothrombin only if the sole variable in the system under test was prothrombin, and this was by no means certain, the term prothrombin was placed in inverted commas in the work indicated above[14] and it was emphasized at a meeting of the Australian and New Zealand Association for the Advancement of Science[15] where it was stated: "It is possible, of course, that the substance causing increase in clotting is not prothrombin but some other coagulant". That there is another substance increasing the speed of clotting in the prothrombin test was soon well demonstrated by Fantl and Nance[1][2] who separated prothrombin from normal oxalated plasma, and have indicated that for rapid thrombin formation another factor called prothrombin accelerator is required, which is present in the globulin fraction. Owren[3] described a hæmorrhagic tendency due to lack of this principle which he termed "factor V". Thus the prothrombin as estimated by the prothrombin time is really a prothrombin "equivalent" since more than one variable is involved. Also recently it has been found[12] that the stable prothrombin component of this system is also composed of two fractions (now called A and B), one related to vitamin *K*, and the original labile component (A) is called "labile factor".

At first it may be thought that such a complication invalidates the test in that we are only determining the activity of a system, not of prothrombin. While this is true, from the clinical standpoint it might be more valuable to assess the activity of the prothrombin system when dicoumarol therapy is given, rather than prothrombin itself, since it is activity of the prothrombin rather than its concentration which we require to reduce in producing satisfactory therapy. Thus if the globulin activator content is low the need to reduce the prothrombin content itself greatly might not be nearly so important as when the globulin activator content is high.[1] Further, once we make an estimation in a particular way we can empirically determine what are the safe limits, and anomalous clinical findings in relation to the first would indicate whether the method is unsatisfactory. If the schedule as outlined below is followed, safety should be ensured. So far using this test we have noted untoward effects only where the prothrombin has been reduced to anything from 5% to 15%. Frequently with a prothrombin level of 6% and even less there have

[1] A method for assay of the labile factor has now been developed. (A. J. Quick and M. Stefanini, *The Journal of Laboratory and Clinical Medicine*, Volume XXXIII, 1948, page 819.)

been no untoward symptoms. Heparin, when used concurrently, sometimes accounts for the low figure if tested within eight hours. In one instance a patient developed profuse vaginal hæmorrhage ten days after Cæsarean section while being treated with dicoumarol (and heparin earlier) since she had developed a pulmonary embolus. At this time the prothrombin level was 34%, but we cannot be sure that the bleeding was due to anticoagulant therapy. Later with a prothrombin percentage of 25 there was no bleeding.[1]

While many modifications of Quick's technique have been introduced, the one that has most practical value is probably that of employing a diluted plasma (as indeed is indicated in Quick's graph) and using this to determine the prothrombin concentration rather than undiluted plasma in the first instance. It is noted (Figure I) that from 50% to 100% prothrombin concentration there is little change in prothrombin time when undiluted plasma is used and so the test in this range is not flexible. In carrying out the estimation in this laboratory over the past few years, a 10% solution of plasma in saline has been used. The thromboplastin is made up as described by Quick.[9] Some workers prefer to use a 50% solution for this test. The volume of each reagent and also of the plasma sample used in the test is 0·2 millilitre, the whole being kept in a large water bath at 37° C. It is essential that the calcium be made up by titration.

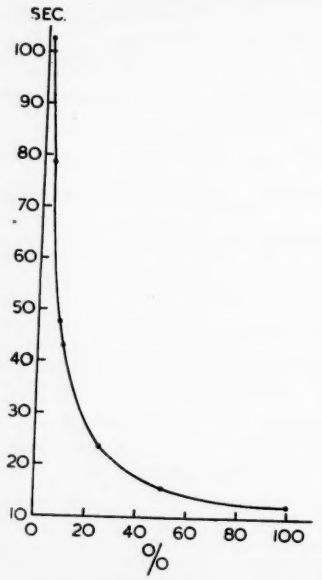

FIGURE I.

Graphical representation of prothrombin time compared with prothrombin concentration. Ordinate: Prothrombin time (seconds). Abscissa: Percentage concentration prothrombin.

Prothrombin Test Carried out on Patients under Dicoumarol Therapy.

When patients are given dicoumarol therapy as for postoperative thrombosis or for coronary occlusion, various differences as to the required prothrombin level are advanced by different workers, probably not because of a difference with regard to the desired clinical response wanted in the patient, but because local differences in technique may give different estimates of the prothrombin content. Those who prefer lower figures in general regard a percentage prothrombin content above 30 as too high for satisfactory clinical response, a percentage content below 20 as too low and a percentage down to 10 as dangerous. There are many who like the figures a little above these. Most workers desire to keep the prothrombin level low for four to five weeks or longer, but from the physiopathological standpoint there seems little advantage in keeping it low for longer than ten days after the last thrombosis if the patient is then mobile.

From the practical point of view it is therefore advised that the plasma should be estimated for prothrombin time in a 10% solution and the concentration of prothrombin can be read readily from the graph (Figure II) in which the abscissa is logarithmic. The graph is prepared from a normal plasma value (*vide infra*) taken as 100 and diluted to give a varying concentration. It is admitted that since we are also diluting other constituents of the prothrombin system such a graph does not necessarily give as true an estimate as when the prothrombin itself alone is diluted, but for the reason stated above, it is considered satisfactory. Thus multiplication by ten does not give a very accurate figure, but at such a concentration the patient is not in the danger range. It is possibly because of these multiple factors that even on logarithmic paper the curve is not a straight line, but sigmoid. The prothrombin content is then estimated from 100% down to 20%. If the prothrombin time is over 100 seconds (less than 22%) it is then wise to carry out tests on neat plasma which now is in the flexible range 2% to 20%, and it is to be remembered that in a number of these cases coagulant therapy may be advised. This, then, gives the times shown in Table I. In this way a fairly sound estimate of the prothrombin "concentration" can be given. Again by plotting on logarithmic paper the amounts are estimated more easily (Figure III).

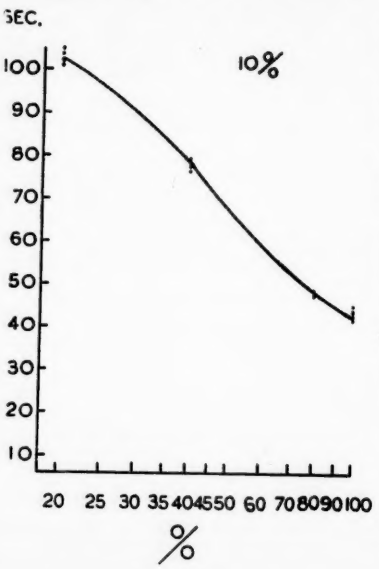

FIGURE II.

Graphical representation of prothrombin time compared with prothrombin concentration when 10% plasma is used: logarithmic paper. Ordinate: Prothrombin time (seconds). Abscissa: Percentage prothrombin (logarithmic).

Selection of Normal Plasma.

Apart from the activity of the thromboplastin, frequently apparently normal people do not yield plasma indicating 100% (standard) prothrombin. It is necessary to test plasma from several healthy people and when this is done, it is found that there is a group of plasmas at the maximum concentration of prothrombin which give extremely close values for neat plasma and 10%. The correspondence of the neat and the 10% plasma multiplied by ten is important. In our experience the first thromboplastin extract to be made gave low readings for all plasmas, but with experience it was found that the second, third, fourth, fifth and sixth batches were very satisfactory as regards their constancy. Quick[11] has further commented on this. In our hands a plasma is selected which produces a prothrombin time (neat) of 12·0 to 12·6 seconds and prothrombin time (10%) of 41·3 to 44·7 seconds. Plasma is obtained from four or more healthy people and if the maximal plasma values fit with this time, the extract is considered satisfactory; but if they are below, it is discarded. The constancy of these findings is well shown in Table II. Set dilutions of plasma were tested which show extremely good agreement. It is considered that such a selection enables a valid test to be carried out in spite of the complicated nature of the prothrombin reaction. The extract is so tested weekly and discarded after a fortnight after being kept in the cold. Hyperprothrombinæmia occurs in methylxanthine therapy[3] and following vitamin *K*,[4] but this is denied by Nitshe, Gerarde and Deutsch. Some consider it is found in patients about to develop thrombosis.[12]

[1] Clinical details through the courtesy of Dr. Robert F. West.

Assay of Prothrombin Content in Cases of Abortion.

A patient, in whom an abortion was threatened, was examined by one of use (E.R.T.) in 1941 and it was considered that the clinical history was probably significant.

The patient (married) was desirous of having a child and there was no suggestion of interference. In spite of care by senior obstetricians abortion followed at the thirteenth week.

TABLE I.

Percentage "Prothrombin" Compared to Prothrombin Time with Undiluted Plasma.

Percentage "Prothrombin".	Prothrombin Time. (Seconds.)
2	103
4	78
6	60
8	49
10	42
12	37·5
14	34
16	31
18	28·5
20	27

Some months later, after the patient had recovered, pregnancy was again desired, but following conception bleeding recurred. The bleeding was intermittent and at times severe, and after the tenth week the obstetrician in charge felt that an abortion would again supervene. About a week later a severe hæmorrhage occurred and on examination it was noted that the patient also had some bruises. Since it

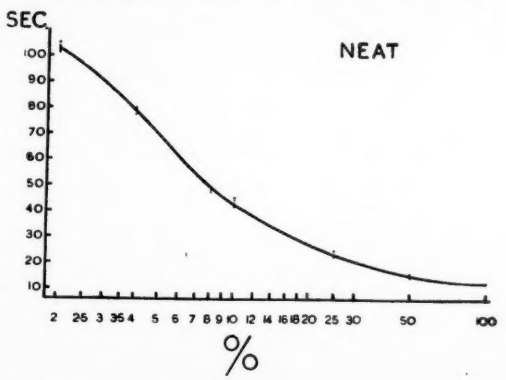

FIGURE III.

Graphical representation of prothrombin time compared with prothrombin concentration when neat plasma is used: logarithmic paper. Ordinate: Prothrombin time (seconds). Abscissa: Percentage prothrombin (logarithmic).

was not possible at this time to carry out a prothrombin estimation and the patient was in considerable distress at the thought of losing the second fœtus, synthetic vitamin *K* (prepared by Dr. Fantl of the Baker Institute) was dissolved in olive oil (10 milligrammes per millilitre) and 1·0 millilitre of the solution was rubbed thoroughly into the thigh till absorbed. Later doses were given on the two following days. Within six hours of the first inunction the bleeding ceased and throughout the remainder of the pregnancy no more bleeding occurred. Later in pregnancy further doses were given. A normal child was delivered at term. A little over a year later pregnancy was again desired and following conception 1·0 millilitre of synthetic vitamin *K* dissolved in olive oil (10 milligrammes per millilitre) was inuncted weekly for some weeks, and again in the latter part of pregnancy. No bleeding whatever occurred in this pregnancy and a normal child was delivered at term.

It may, perhaps, be not without significance that this patient had an aversion to cabbage, a potent source of vitamin *K*, though admittedly intestinal bacteria are an important source of the vitamin. While we cannot say in this case owing to lack of laboratory investigation that vitamin *K* deficiency was present, the clinical story is suggestive. Further work has now shown that in any case a simple prothrombin test, as available at that time, would not have proved conclusively a deficiency in vitamin *K*, though it might have indicated deficiency of the prothrombin system.

TABLE III.

Plasmas from Patients with Early Abortion Tested for Prothrombin Content (Neat Plasmas and 10% Dilution).

Patient Number.	Prothrombin Time (in Seconds).								Percentage Prothrombin.
	Neat.				1/10.				
1	13·5	13·6	13·6		59·1	59·2			60
2	13·4	13·8	13·5		55·0	55·4	54·8		66
3	11·8	11·9	11·9		34·0	34·0	33·8		126
4	14·4	14·3	14·2		60·0	59·0	59·5		60
5	13·4	13·5	13·4		54·3	54·0	54·1		68
6	18·6	18·5	19·0		75·0	74·0	75·0		43
7	14·9	14·4	14·3		57·0	56·5	56·2		64
8	15·0	15·0	15·0		52·4	52·5	52·8		70
9	14·4	14·2	14·1		54·0	53·8	53·9		68
10	15·5	15·8	15·9		69·4	69·5	69·4		49
11	14·0	14·8	14·5		48·5	49·5	49·6	49·9	77
12	13·8	13·9	13·4	13·5	39·4	37·9	38·0		112
13	14·8	15·1	15·0		57·0	56·8	57·1		63
14	14·0	13·8	14·1		45·3	45·4	45·3		86

It was then thought worth while to determine if early abortion might be related to vitamin *K* or prothrombin deficiency in some cases. The great difficulty, of course, is to exclude interference, and while the first physician who attends such a patient after interference has been undertaken is frequently told the truth about the situation, when another physician comes in at a later stage to carry out tests on such patients, it is exceedingly difficult to obtain honest information. Owing to the exigencies of the war situation, this work was not carried out until some years later.

In the meantime artificial deprivation of vitamin *K* in rabbits was found to cause abortion.[6] Later a paper was published by Javert and Stander[5] in which evidence of prothrombin deficiency was given in cases of abortion. These were classified as threatened, spontaneous (when one or two previous abortions had occurred), and habitual (when three consecutive abortions had occurred). The prothrombin content of the blood averaged 65%, 46% and 61% as against practically normal values on the average in early pregnancy without abortion. In view of the response to treatment *plus* the evidence of these figures, it was considered that vitamin *K* deficiency played a part in early abortion. On the contrary no mention is made as

TABLE II.

Comparison of Different Samples of Thromboplastin (Quick) (2 to 6) Tested Against Selected Plasma (1 to 5) also Diluted.

Dilution.	Sample 2, Plasma 1.			Average.	Sample 3, Plasma 2.			Average.	Sample 4, Plasma 3.			Average.	Sample 5, Plasma 4.			Average.	Sample 6, Plasma 5.			Average.	Combined Average.
Neat	12·1	12·0	11·9	12·0	12·4	12·5	12·8	12·6	12·5	12·3	12·4	12·4	12·4	12·3	12·3	12·3	12·4	12·8	12·6	12·6	12·4
50%	15·4	15·6	15·4	15·5	16·0	16·2	16·3	16·2	16·1	16·0	15·7	15·9	16·0	15·8	15·8	15·9	15·8	15·7	15·7	15·7	15·8
25%	21·8	22·4	22·3	22·2	24·4	24·5	24·6	24·5	24·0	23·8	—	23·9	24·0	23·9	—	24·0	22·6	22·8	22·5	22·6	23·4
10%	41·2	41·4	—	41·3	43·1	43·2	43·5	43·3	44·5	44·7	44·8	44·7	42·3	42·1	—	42·2	43·4	43·2	43·5	43·4	43·0
8%	47·8	48·1	—	48·0	46·8	47·0	47·1	47·0	47·1	47·2	47·0	47·1	45·8	45·9	45·6	45·8	46·8	47·2	47·3	47·1	46·0
4%	78·4	78·8	—	78·6	80·0	79·8	79·9	79·9	77·0	77·1	77·3	77·2	76·9	76·5	76·4	76·6	78·1	78·3	78·2	78·2	78·1
2%	101·0	101·4	—	101·2	104·2	104·8	104·6	104·5	101·4	101·8	—	101·6	104·8	105·1	—	105·0	102·1	102·3	—	102·2	102·9

TABLE IV.
"Prothrombin" Concentration in Abortion.

Number.	Induced Percentage Prothrombin.	Number.	Spontaneous Percentage Prothrombin.	Number.	"Probably Induced" Percentage Prothrombin.	Number.	"Possibly Spontaneous" Percentage Prothrombin.
6	43	4	60	7	64	1	60
10	49	5	68	11	77	13	63
2	66	12	112	3	126	9	68
8	70	—	—	—	—	14	86
Average ..	57	—	80	—	89	—	69

to how evidence of mechanical interference was excluded. It would certainly be necessary to carry out tests on such a group to exclude the importance of hæmorrhage or some other factor which might indicate a difference between cause and effect. In the findings about to be recorded this inquiry was made. A series of patients suffering from early abortion were interviewed by one of us and a decision was reached as to whether there was a mechanical cause for the abortion and the other performed the prothrombin test. The following were the findings recorded in Table III.

In Table IV in the first column are placed the percentage findings for the patients who readily admitted interference. In the second column are the figures when the abortion was considered spontaneous. This can be only an opinion, however well founded. In the next column the figures are recorded for the patients when it was considered induction was probably performed and in the final column when it was thought that possibly the condition was spontaneous.

While it is not certain that the cases designated spontaneous actually are, it is obvious that there is frequently a low "prothrombin" content of the plasma in cases of induced abortion, and therefore unless there was an exceptionally low group of "prothrombin" figures, it would be difficult to assess if there was any further deficiency contributing to abortion in the early weeks of pregnancy, these cases occurring in eight to fifteen weeks. It is possible that the method of inducing abortion may affect the prothrombin content of the blood. On the other hand it is not unlikely that the hæmorrhage, which is quite commonly severe in these cases, may be responsible for the low "prothrombin" figures and, therefore, this investigation has yielded no positive information of low prothrombin content of the blood as a predominating cause of abortion. If a low prothrombin content was found to precede a threatened or spontaneous abortion before any bleeding occurred, the evidence would be more conclusive. While vitamin *K* deprivation will cause abortion in rabbits, we cannot yet state the relative importance of such deficiency as a causal factor in spontaneous abortion in humans.

Summary.

The 1940 prothrombin test of Quick has been considered in relation to dicoumarol therapy.

The clinical history of a patient who developed abortion and in whom vitamin *K* therapy was applied is described, and the prothrombin content of the blood of patients who had aborted has been determined.

Acknowledgement.

Thanks are due to the honorary staff of the Royal Adelaide Hospital for access to patients.

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STREPTOMYCIN IN TUBERCULOSIS.

By J. BELL FERGUSON, V. G. BRISTOW and P. R. BULL,
Austin Hospital, Melbourne.

OVER four and a half years have passed since Schatz, Bugie and Waksman first presented streptomycin as an antibiotic in America. Shortly after this Feldman and Hinshaw showed that streptomycin possessed a unique bacteriostatic action against the tubercle bacillus, both in small laboratory animals and later in the human subject. Several manufacturing chemists expended large sums in setting up facilities for the preparation of the new drug, and by agreement with these firms, certain centres were chosen for clinical research with the drug. Numerous reports have since been published, the most comprehensive being from the American Trudeau Society, and from the Veterans Administration Streptomycin Committee, in January, 1948. Despite the many hundreds of patients with various types of tuberculosis who have been treated with streptomycin, its place in the treatment of this disease has not yet been completely settled.

In August, 1947, the Victorian Government made available a sum of £5000 for the supply of streptomycin. The first supplies were used at the Austin Hospital, but later

limited quantities were made available to Gresswell, Greenvale and Heatherton Sanatoria, to the Queen Victoria Annexe, Mint Place, and to some chalets attached to base hospitals throughout the State. Cases were selected as suitable by a small voluntary committee of three physicians and two surgeons, who were provided with a short history of each case with X-ray films.

Route of Administration.

In practically all forms of tuberculosis the method of choice is by parenteral injection. In some cases of laryngeal tuberculosis aerosol inhalation was used, but appeared to have no appreciable advantage over the parenteral method.

In tuberculous meningitis, daily intrathecal doses of 25 to 100 milligrammes in addition to intramuscular injections have been used. Even now some doubt has arisen as to the real necessity for the intrathecal administration. Complications met with in cases of meningitis may be due largely to its intrathecal use.

Bacterial Fastness.

Tubercle bacilli can develop resistance to streptomycin either *in vitro* or *in vivo*. This raises a very difficult and important problem in its use, because it indicates that we cannot use streptomycin freely for the very type of case in which it should theoretically produce most benefit—namely the early minimal lesion, found for example by microradiographic surveys. The reason is that in a large proportion of cases this "fastness" develops in a fairly short period, forty to sixty days or even earlier. This fastness may be permanent and the bacillus breeds true, so we may be faced with streptomycin-treated patients spreading a tubercle bacillus which will be resistant to the drug. Moreover, the development of fastness limits our use of the drug as an "umbrella" to cover operative procedures. If we use it too soon, we may regret this at a later date when more urgent coverage may be required. Further light is required on this aspect of the drug, for use of different culture media has given different results. When Dubos-Davis media were used 25% of strains were resistant, and when Youman's media were used, 68% were streptomycin resistant. Some standard medium must be sought.

The mechanism of this resistance is not known definitely. It has been stated that resistant and sensitive forms of tubercle bacilli are present in each case from the beginning, and that only streptomycin-sensitive organisms are affected by the drug, the others persisting and growing. It is more probable that the bacilli are sensitive from the beginning and later develop resistance. It is to be hoped that some form of combined therapy, either with a chemotherapeutic substance or with another antibiotic, will solve this important problem of resistance. In the meantime it will be helpful if a standard method of testing cultures from treated patients—(*a*) before, (*b*) during and (*c*) after streptomycin treatment—can be evolved. Work is now proceeding along these lines, and the results will help considerably in the application of streptomycin in our clinical work.

Dosage.

Dosage at first was three grammes per twenty-four hours given in six divided doses, later two grammes, then one gramme; and in July of 1948 this was still further reduced to 0·5 gramme per day in two divided doses. Possibly a single dose of 0·5 gramme would produce the same results. The standard course is for sixty days, a total of 30 grammes. This comparatively small dose seems to give just as good results as the earlier large dosage with a considerable diminution in the occurrence of toxic phenomena.

Toxic Phenomena.

First of the toxic phenomena is loss or decrease of labyrinthine function. With the use of smaller doses such vestibular disturbance is not at all pronounced, and most patients are very well compensated in a few weeks. The persistence of symptoms has been reported only in patients receiving prolonged treatment with large doses.

Secondly, slight albuminuria may be noted, with the passage of a few cells in the urine. The risk of renal damage appears to be slight except to patients with previous renal impairment.

Thirdly, a few allergic reactions have been noted, chiefly confined to morbilliform rashes, sometimes with fever which yields to antihistamine drugs such as "Benadryl". As a rarity, exfoliative dermatitis has been described. Toxic phenomena seem to be definitely related to the size of the dose, and with doses of one gramme per day or less a few reactions are to be expected. Cases of contact dermatitis in those handling streptomycin have been described, and staff should be warned to use reasonable care and wear rubber gloves for handling any quantity of the drug.

TABLE IA.[1]
Early Results of Treatment of 113 Patients.

Patients.	Effect on Lesions Assessed Radiographically.			Total.
	Condition Improved.	Condition not Improved (Including Early Relapse).	Condition Worse (Including Early Relapse).	
Austin Hospital patients.	26	5	3 (including 2 deaths)	34
Patients from other institutions.	55	18	6 (including 1 death)	79
Total ..	81 (72%)	23 (20%)	9 (including 3 deaths) (8%)	113

TABLE IB.[1]
Early Results of Treatment of 113 Patients.

Patients.	Effect on General Condition of Patients.			Total.
	Improved.	Not Improved (Including Early Relapse).	Worse (Including Early Relapse).	
Austin Hosptial patients.	28	3	3 (including 2 deaths)	34
Patients from other institutions.	62	12	5 (including 1 death)	79
Total	90 (80%)	15 (13%)	8 (including 3 deaths) (7%)	113

[1] Tables IA and IB give a summary of the response of these patients in the first two or three months following institution of treatment, which was carried out for an average period of sixty days. To assess the early results of streptomycin treatment we have used two different sets of criteria, namely the change in the radiological appearance of the lesions, and the change in the patient's general condition as manifested by the temperature and pulse charts, alteration of symptoms, change in weight *et cetera*, examination of sputum and blood *et cetera*. It will be seen that streptomycin treatment resulted in an improvement in the radiological appearances in 73% of cases and in an improvement in the patient's general condition in 80% of cases.

Types of Pulmonary Tuberculosis Treated.

The types of pulmonary tuberculosis in which streptomycin was used may be grouped as follows: (i) Cases in which the lesion was in an acute exudative phase. (ii) Cases in which a new exudative lesion or a reactiva-

tion of an old lesion immediately followed some surgical procedure. (iii) Cases in which pulmonary lesions indicated the necessity of some form of surgical treatment, but in which the extent of the lesions and the toxic manifestations rendered the patients "bad risks". (iv) Cases of tuberculous tracheobronchitis or tuberculous laryngitis.

Results of Treatment.

We have personally observed 43 patients suffering from pulmonary tuberculosis treated with streptomycin, and we have had reports from other sanatoria and chalets of a further 70 cases, a total of 113 cases in all. In Table I are set out the early results of the treatment of the 113 patients.

The patients for whom streptomycin was used as the sole method of treatment showed 100% initial improvement. It may be stated here that all these patients were carefully selected, and in every case there was a specific indication for the use of streptomycin, such as acute exudative lesion without cavitation, or tuberculous tracheobronchitis with negligible radiological evidence of parenchymatous lung disease. However, at the end of an average period of eight and a half months, six of the 13 patients had relapsed. This is an alarming percentage of relapses, and is much the same as that found by our colleagues in other institutions.

TABLE II.
Follow-up Investigation of 43 Austin Hospital Patients.[1]

Type o Streptomycin Therapy.	Initial Improvement.		No Initial Improvement.		Total.
	Improvement Maintained.	Relapse.	No Change.	Condition Worse.	
Sole treatment of tuberculosis ..	7	6	—	—	13
Adjunct to collapse therapy or pulmonary resection:					
Spread or reactivation..	9	—	—	—	9
Preparation for collapse or resection ..	18	1 (died)	1	2 (died)	22

[1] Includes 34 Austin Hospital patients *de novo plus* nine transferred from other institutions to Austin Hospital, to whom streptomycin had been given prior to admission to Austin Hospital. We have followed up 43 patients for periods of up to twenty-two months and for an average period of eight and a half months. Table II shows the results in these cases. This group can be further divided into those cases in which streptomycin was used as the only method of treatment apart from rest, and those cases in which it was combined with some form of collapse therapy or pulmonary resection.

In the second group of cases in which streptomycin was used as an adjunct to some other form of therapy, and in which it made possible many operations on patients who would otherwise have been unsuitable for surgical treatment, the initial improvement was 93%, and what is most significant, only one patient has so far shown relapse, and this patient has died. Of the two patients who showed no initial improvement, one has died and the condition of one remains unchanged.

Summary of Indications for the Use of Streptomycin.

The following facts on the use of streptomycin seem to emerge from our own experience and from the literature, which is already voluminous and somewhat confusing.

1. Streptomycin treatment is a true therapeutic measure in quite a small proportion of cases of tuberculosis, although the drug will give some apparent relief in almost any type of case.

2. The facts which militate against its widespread use are that there is a high relapse rate when the drug is used alone, and that in a large proportion of cases the bacillus develops resistance to the drug and this resistant strain tends to persist. Spread of such resistant strains would at present prove a menace to the general population, and it will remain so until we develop an antibiotic or other drug which will control such resistant strains or act itself without producing resistant strains.

3. Streptomycin is indicated in the control of recent active tuberculous lesions of the exudative type, irrespective almost of the extent of such lesions.

4. It is of great value as an "umbrella" or safeguard against spread in major chest surgery in lung tuberculosis, and we have used it particularly in this type of case with good results.

5. Thus its use should always be considered carefully in relation to any possible surgical programme to be carried out, and its administration withheld until that programme can be arranged.

6. In acute spread occurring after major surgical procedures, in bronchogenic spread, or in bronchopneumonia, its use without delay is strongly indicated; but the principle stated in paragraph 5 should be borne in mind.

7. In bronchial tuberculosis with ulceration, especially when lesions are clearly seen at bronchoscopy, initial results are excellent in most cases; but when parenchymatous disease is present, relapse is almost inevitable unless streptomycin treatment is combined with pulmonary resection.

8. In chronic cases great relief is obtained in conditions such as tuberculous ulceration of the larynx or pharynx and tuberculous enteritis.

9. Patients with sinuses of various types may benefit, particularly sinuses from bone lesions which have become quiescent. The use of streptomycin in empyemata, closed abscesses, broncho-pleural fistulæ and active bone lesions gives disappointing results.

10. Streptomycin should not be given when extensive "breaking down" is taking place in the lung lesions, or when fibro-cavernous or fibro-caseous conditions are present, unless in conjunction with surgical treatment.

11. If it is to be helpful, streptomycin therapy will produce favourable indications in three or four weeks. If this does not take place, there is little use in persisting with the drug.

Conclusion.

Streptomycin does not, and should not be expected to, replace the well-tried methods of bed rest and the various well-tried procedures of collapse therapy. Rest is still the keystone of successful treatment of tuberculosis.

Acknowledgements.

We should like to express our thanks to the medical superintendents of Gresswell Sanatorium, Greenvale Sanatorium and Heatherton Sanatorium, and to the medical officer of the Queen Victoria Annexe, to the medical officers of the chalets at Bendigo, Ballarat, Wangaratta, Sale and Hamilton, and to Dr. Frank Kerr, Commonwealth Medical Officer, who acted as chairman of the State Streptomycin Committee, for information concerning their patients treated with streptomycin.

INDUSTRIAL DERMATITIS.[1]

By EDWARD ROSANOVE, M.R.C.P., M.R.A.C.P.,
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ON the subject of industrial dermatitis and all its ramifications numerous volumes have been written. It is not my intention to discuss the effects of various industries on the skin, but rather to give a general account of some of the very difficult problems that confront the consultant when he comes up against a case of industrial dermatitis. These problems include the questions of ætiology, diagnosis, prognosis, treatment and prevention.

[1] Read at a meeting of the Section of Dermatology and Industrial Medicine, Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1948.

We must first of all get, if we can, a clear conception of the differences between the terms "dermatitis" and "eczema". Sequeira considers that dermatitis includes all skin inflammations due to mechanical, chemical, microbic or parasitic irritation, the types of neurodermatitis and the essential prurigos. Urbach says: "Idiopathic eczema is hypersensitivity primarily affecting the blood vessels; occupational eczema primarily affects the epithelium." Urbach, as you see, uses the term "eczema" in both senses. There are eminent dermatologists who deny that such a condition as endogenous eczema exists at all.

If we state that dermatitis includes that group of cases which are due to direct contact with an external irritant, and the term eczema is limited to endogenous cases, then we have the extraordinary instance in which identical clinical and histological conditions are given different names purely on an ætiological basis. To the best of my knowledge that does not occur anywhere else in medicine. Nevertheless we must, for the sake of uniformity and clarity, stick to that differentiation.

A case of dermatitis, then, is due to contact with an external irritant; therefore, the more irritant the contact and the more sensitive the skin, the more likely is there to be a resulting dermatitis. Apart from the well-known tendency of the red-haired or very fair patient to react adversely to irritant contacts, it is considered that the seborrhœic and the hyperhidrotic are also much more likely to be prone to contact dermatitis.

In these facts is there not some clue which might help us to prevent industrial dermatitis up to a point, particularly in well-known hazardous trades? Would not a medical examination prior to employment be of considerable benefit? Preliminary patch tests are not very helpful and are somewhat impracticable. As a rule, sensitivity takes days or weeks to develop, and again, conditions at work—heat, sweating and friction—are factors which occur at work but which are absent in a patch test. The prevalence of industrial dermatitis is well known. Prosser White quotes reports from all countries in the world, and the relative prevalence of occupational dermatitis to all other skin diseases varies from 2% to 20%. This great variation is due to a great number of factors, not the least of which are the diagnostic skill of the medical attendant and the prospects of compensation. We have all dealt with cases referred to us by insurance companies that are not and cannot, in any way, be due to the occupation—such as *pityriasis rosea*, scabies and so on.

While I am on this point I should like to say how strongly I feel against the medical man who thinks that, because he is acting for insurance companies, he must be biased in their favour and makes every effort to turn down a case. I can quote a number of instances in which this has happened; very often the patient suffers when he should be getting compensation. At times the victim takes it to his union, who will fight the case, and then it goes to arbitration, and we have the unedifying spectacle of two so-called experts flatly contradicting each other.

The insurance companies, I am sure, do not want biased opinions. In the long run it must pay them better to have honest, unbiased opinions.

Statistics show, and any dermatologist can confirm this from his own practice, that the most hazardous occupation is that of the housewife—the hazard most commonly being due to soap and soap extracts. The frequency in different trades varies in different countries, but Prosser White's list is interesting. It is, in order of frequency, household workers, labourers, painters, metal workers, mill hands, oil and grease workers, physicians, dentists and nurses, cloth handlers and weavers, bakers, tanners and leather workers, chemical and dye workers; and the relative frequency of the different injurious agents is as follows: alkalis, sugar, oil, chemicals, turpentine and substitutes, dyes, dough, paraffin, friction and heat, petrol, chrome, acids, French polish, nickel and accelerators.

The differential diagnosis of a case of occupational dermatitis is at times extremely difficult.

Quite often, I am sure, a great number of cases we see are due more to the cleansing agents used on the hands, such as sandsoap, turpentine and petrol, than to contact irritants. There was an epidemic of dermatitis in an engineering firm in Melbourne. The firm's medical man asked me if I could help. I visited the factory and went through every department. There were some departments where irritants were being handled, but cases of dermatitis were occurring in all departments. We therefore instituted a routine of cleaning the hands and arms. No employee was allowed to use any chemical or mechanical cleanser. The company provided a sulphonated oil with a wetting agent for cleansing, and the dermatitis stopped.

An accurate history is essential, in which is detailed every step in a man's work, every item, chemical or otherwise, that he contacts. It is important to visualize exactly his daily routine.

Sutton and Sutton quote what Sulzberger and Finnerund state are the important criteria for proof of the industrial nature of dermatitis:

> 1. *Inception.* The condition appears at any time during a period of industrial exposure or even after a lapse of a reasonable incubation period following cessation of exposure up to a maximum of two or three weeks.
> 2. *Amelioration.* The dermatitis regularly disappears or is repeatedly improved within a reasonable period of days, weeks or even months after cessation of the causal agent.
> 3. *Recurrent Exacerbations.* The dermatitis tends to recur or exacerbate when the worker returns to the identical exposure.

They then mention other points that have to be noted. (i) The dermatitis appears first in areas of maximum exposure and is usually confined to them; in a few instances it may spread to unexposed areas. (ii) The character and localization of the dermatitis correspond to those in other cases known to have been caused by the same industrial hazards. (iii) A patch test with the offending irritant made on an unaffected area close to the affected sites produces a reaction if made during the active phase or shortly after. (iv) The cutaneous test produces a dermatitis reaction which is similar to the rash. (v) Other workers similarly occupied are or have been similarly affected. (vi) The dermatitis appears within days or weeks of starting a new job.

Errors in considering the condition to be non-industrial may arise from: (i) the finding of fungi or other micro-organisms in scrapings; these may be universally found in normal skins; (ii) negative results from patch tests with the suspected irritant; these may be due to the testing of different areas, with consequent local differences in sensitivity, to testing with the wrong substance, to use of the substance in weaker form, and to absence of the working conditions, such as heat, sweat, friction *et cetera*.

Errors in diagnosing the condition as industrial may arise: (i) if a rash occurs on a person in an industry notorious for the occurrence of dermatitis; it may be due, for example, to exposure at home to cosmetics, paint, plants *et cetera*; (ii) if the result of a patch test is positive; this is not conclusive because it never accurately reproduces the conditions of actual exposure.

These important criteria should give one a fairly definite opinion as to whether the condition is an example of industrial dermatitis or not. Clinically, it is important to eliminate such conditions as seborrhœic dermatitis, *pityriasis rosea*, scabies, disseminated neurodermatitis, the true allergic eczemas and, one of the most difficult of all, cheiropompholyx of the hands.

The employee who develops a rash at work, particularly if it is a noxious trade (dermatologically speaking), always considers that it is due to his work. If a definite clinical entity, such as *pityriasis rosea* or scabies, is found, as it very often is, then it is easy. Difficulty is found with cases of neurodermatitis, eczema and cheiropompholyx. Then we must use our judgement from the history and clinical appearance of the condition. What is the position of the patient who is a true sufferer from allergic eczema and whose condition is activated and aggravated by his occupation? I consider that he is definitely entitled to compensation and treatment until his rash is at least quietened.

Prognosis.

Removal of the cause is usually followed in a few days or weeks by complete recovery. There are conditions that remain chronic for some months and at times these develop into eczema. I am sure that autointoxication can occur with sensitization of the skin elsewhere and chronic generalization will develop, such as is very often seen in cases of varicose dermatitis. Efforts at desensitization are, as a rule, unsuccessful. Sensitivity may disappear if contact is avoided for a few months, or the degree of sensitivity may diminish. Usually sensitivity remains undiminished throughout life and contact with the allergen means a recurrence. I also think that sensitivity can develop even after years of freedom. I think we all see this quite often, and logically it must be right to say that the longer you contact an irritant, the more likely you are to become sensitive eventually.

Often a skin sensitized to a specific allergen will develop a sensitivity to other allergens. If an affected person changes his job, as he often has to, he must be careful what new occupation he chooses. I have seen a carpenter change to a milkman and become very soon sensitive to milk.

Treatment.

The treatment in a case of industrial dermatitis does not, as a rule, present any difficulties. Once the contact is avoided, the irritating factor is removed and with routine treatment the condition rapidly subsides. As in all cases of dermatitis, care must be taken to avoid over-treatment. As you know, reputations are made by the use of calamine lotion and zinc cream. Small doses of superficial X-ray therapy and mild sedatives are beneficial.

Prevention.

The economic question due to industrial dermatitis is a very large one. The following are suggestions I should like to make about steps that could be taken to reduce the incidence of this condition.

1. Evaluation should be made of the degree of irritation of various contacts in an industry. Materials with a high sensitization index should not be used in industry if they can be replaced by other materials not possessing such potentialities.

2. New chemicals should be tested before use to determine their sensitizing index.

3. Persons with skin diseases, such as acne (in hot, sweaty occupations), seborrhœic dermatitis, hyperhidrosis and ichthyosis, should not be employed in dermatologically hazardous occupations.

4. Preemployment patch testing is probably impracticable. It has been suggested that testing with adhesive plaster is easy and useful, since those sensitive to adhesive usually have a polyvalent sensitivity and frequently react to other sensitizing substances.

5. Once a patient has been sensitized to an irritant he should not be allowed to return to work associated with that irritant. If possible, he should be moved to another department or, if necessary, to another occupation altogether.

6. The employer should provide a well-built, airy factory containing the best methods for the complete and rapid removal of all fumes, gases and noxious fluids.

7. Suitable protection for the hands, if practicable, should be provided for each employee.

8. The various barrier creams, both oil-protective and water-protective, should be tested out in every factory and their value estimated in each industry against all irritants. This was of great help in reducing the incidence of industrial dermatitis in the war factories in England.

9. Facilities for scrupulous cleanliness must be provided for every employee. As I said before, the use of sand-soap and chemical cleansers must be strictly forbidden. The provision of the sulphonated oil cleanser is, I think, a necessity, it being remembered, however, that we strike an odd case of sensitivity to this also.

THE NATURE, RECOGNITION AND TREATMENT OF GLAUCOMA.[1]

By ARTHUR D'OMBRAIN, M.B., Ch.M., D.O.M.S., F.R.A.C.S. (Oph.),

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THE presentation of a scientific subject, may be made in two ways: (i) objectively, giving, as far as one can, the summation of known and generally accepted knowledge of the subject; (ii) subjectively, giving one's own personal views and experiences.

Each of these approaches has its advantages and disadvantages. The first is more reliable as a general guide but does not tend to produce much advance in conception, either of nature or of treatment. The second approach is less reliable, for an individual worker may be either wholly or partially mistaken in his point of view and conclusions, but whether this is so or not, interest is stimulated and critical thought aroused.

In this paper I will try to treat the recognition of glaucoma objectively, its nature mainly subjectively and its treatment with an admixture of both approaches.

Also, I must ask you to bear with me if I deal with recognition and treatment rather sketchily, in so short a paper on such a vast subject, for my main purpose this evening is to put before you some reflections upon the nature of primary chronic glaucoma.

Recognition.

Clinically, there are two main forms of glaucoma, primary and secondary. Primary glaucoma is divided into two groups, acute congestive and chronic; personally, as a result of my own investigations into a special type of glaucoma, to which I shall briefly refer later, I divide secondary glaucoma also into acute and chronic groups.

But recognition of acute and chronic glaucoma, whether primary or secondary in origin, is dependent upon the observation of a group of characteristic symptoms and signs. As with any disease of problematical ætiology, theories, methods, interpretations and conclusions are legion, even the very terminology varying as the wind which bloweth where it listeth.

Despite, however, all these variations and whether we look upon glaucoma as a disease *sui generis* or as a symptomatic condition, there is one common characteristic and that is an increase in the intraocular pressure; it is from this phenomenon that all symptoms, signs and sequelæ of glaucoma derive, and it is in the light of this that we must try to understand these signs and symptoms.

Acute Glaucoma.

Recognition of an attack of acute glaucoma is often easy, but, as in all medicine and surgery, there are sometimes traps and not only for young players. Bearing in mind our cardinal characteristic, that of an abnormal pressure within a hollow viscus, the first and most constant symptom is the same as it is in any other over-filled cavity in the body, be it the heart, the bladder or the skull. This symptom is pain; it is severe, unremitting and prostrating pain. As in the case of rapidly increasing intracranial pressure, or almost any intravisceral hypertension, this pain is accompanied by nausea or vomiting. This distinguishes it from the pain of acute iritis, which is of a different nature; you might compare the pain of iritis with that of the pain of dental caries and the pain of acute glaucoma with that of an apical abscess.

Ask the patient about it; if he can speak at all, there will be no fancy phrases; he will say: "The pain, doctor, the pain." The other main symptom is reduction of vision, even to complete blindness in the affected eye or eyes. This symptom is caused by pressure effects upon the laminated corneal epithelium, and hence you get the first sign, haziness of the cornea. The pupil, except when the condition is

[1] Read at a meeting of the Royal Australasian College of Surgeons, in Sydney, on February 28, 1949.

secondary to iritis with complete posterior synechiæ, is dilated and immobile. The eyeball is engorged and tender, and it is as hard as a stone.

The difficult cases are those secondary to iritis, in which you have the constricted pupil typical of iritis but still the specific symptoms of acute glaucoma: the terrible pain due to stretching of sensory nerve endings, the hazy, greenish cornea and the tense and tender globe.

Chronic Glaucoma.

Recognition of chronic glaucoma also is often easy, but detection of early chronic glaucoma is a prize only to be won by the exercise of careful and patient investigation. Main symptoms are a history of rainbow haloes, transient attacks of pain and blurred vision, and a tendency to bump into objects. Main signs are enlargement of the blind-spot or some more gross lesion of the visual fields, cupping of the optic disk, and an increase, as measured by a tonometer, in the intraocular pressure. There are a number of supplementary and provocative tests, which I will just mention: the vascular lability test, the water drinking test, the plotting of the fluctuating diurnal curve, the dark room test, the caffeine test and the determination of the response to mydriatics. These tests all have their place and value, but none of them are infallible.

Treatment.

Acute Glaucoma.

Treatment of an attack of acute glaucoma differs in so far as it may be of a primary or a secondary nature, but in both cases the treatment may be divided into general treatment and local treatment, and in both the general treatment is the same, namely, the administration of morphine, to relieve the devastating pain.

In acute primary glaucoma, morphine serves a second purpose, for by contracting the pupil it helps in opening the angle of the anterior chamber, thus facilitating drainage through the trabecular exit-meshwork in the posterior part of the cornea.

Local treatment in primary acute glaucoma consists firstly in the application of miotics to try to convert the condition from an acute to a subacute or quiescent state. Eserine sulphate in 1% solution should be instilled every half-hour, supplemented by foments, for twenty-four hours. Sometimes I have had success with subconjunctival injections of eserine, but you can easily imagine the difficulty of administering this, except under general anæsthesia. If the condition of the eye is still acute after twenty-four hours, surgical treatment is imperative.

Local treatment in acute glaucoma secondary to the bound-down pupil of iritis, may be summed up in one word: iridectomy, with or without iris inclusion.

Chronic Glaucoma.

My own treatment of chronic glaucoma is influenced by my personal hypothesis, which I shall presently submit to you, that impairment of the drainage mechanism is the dominant factor; but whether my hypothesis that impairment of the drainage mechanism is the dominant factor in all simple glaucoma is true or not, it is nevertheless indisputable that in elderly people the trabecular meshwork tends to become sclerosed. As most of the cases of simple chronic glaucoma which confront us occur in elderly people, it would seem to me justifiable to accept deficiency in trabecular drainage as a major factor in considering treatment or surgery.

It follows from this that the value of miotics as treatment in glaucoma is proportionate to the amount of trabecular filtration still available. If the trabecular meshwork is blocked or nearly blocked, miotics are almost useless. Miotics act by opening the angle of the anterior chamber (if this, too, is not hopelessly clogged or obliterated) and also by causing a vasodilatation of the capillaries of the iris and of the ocular arterio-venous bed. In those cases in which the angle of the anterior chamber and the trabecular exit-network are not hopelessly blocked, miotics can be most efficient, if they are used in adequate strength and with sufficient frequency.

The only way, however, to find out the efficiency of miotics in any particular case of glaucoma is by practical trial. Such trial must be carefully planned; it is not sufficient merely to prescribe eserine or pilocarpine to be instilled three times a day and to hope for the best while fearing the worst. In the planning of the strength and frequency of miotic medication, attention should first be given to the state of the visual fields; the more loss there is found to be, the greater should be the strength of the miotic or miotics, and the shorter the periods between their instillation.

Secondly, the intraocular tension should be measured not less than six hours after the instillation of a miotic; if the tension is found to be unmistakedly higher than normal, then the tension should be measured four hours after the instillation of a miotic of known strength. The point is, of course, that the period for which a miotic will keep the intraocular pressure within normal limits should be ascertained. This period should then be strictly adhered to, even through the night, if this is possible; it is surprising how many people prefer this inconvenience to the frightening prospects and the real or imagined risks of surgical operation.

It having then been ascertained whether an interval of three, four, five or six hours is the correct one, and whether eserine of 0·25% to 0·5% strength or pilocarpine of 1% to 2% strength, or an alternation of both, is the most effective in maintaining a normal tension without causing undue iris spasm, the patient should be put on this routine and kept under observation. If the tension fails to remain within normal limits (I would put 25 millimetres of mercury as the upper limit) and particularly if the visual fields continue to contract, operation should be insisted upon. Otherwise, despite much opinion to the contrary, I see no reason whatever why an elderly patient should not be spared the ordeal and risk of surgery.

If, however, the patient is comparatively young, I think that surgery should be advised, unless the glaucoma is of very slight degree and easy of control.

As to surgery, any success which may be achieved by filtration operations is due, in my opinion, to their providing alternative drainage routes and not to reestablishment of the original channels.

In my experience surgery is much more successful in simple chronic glaucoma than in acute congestive glaucoma; the reason for this, I think, is because in congestive glaucoma the vasomotor factor is of greater importance.

As to the type of operation, it would be presumptuous on my part to lay down any rules, for in surgery there is no rule, only the rules of surgery. An operation that I have found very useful and reasonably successful, and which I have been using for some years in both simple and congestive glaucoma, is a combined basal iridectomy and iris inclusion. A peripheral section is made (I use a keratome, as I do for a cataract extraction) and on withdrawal of the iris, one pillar is cut through; then the iris is torn across at the base, as in the "classical" broad iridectomy; the other pillar is not severed but is left beneath the conjunctival flap.

Nature.

A French ophthalmologist once wrote: "*L'œdème, c'est le glaucome.*" Œdema, that's what glaucoma is; yes, an œdema it is, an ocular Dead Sea, whose stagnant waters, denied adequate outlet, fail to irrigate the thirsting lands around them and choke the very soil that they were meant to nourish. Instead of the sweet fruits of sight, the yield is but the bitter apples of anxiety and diminishing hope, as vision contracts and fades until the last stage when the unhappy victim, having eyes, yet sees not.

The causes of œdema, in any part of the body, are many, and the modern conception of the ocular œdema that we call glaucoma, namely, that it is a local manifestation of general bodily disease, has given rise to so many theories of its origin that glaucoma has come to be looked upon as a many-headed hydra. As with the mythical hydra, when one attempts to simplify the problems by chopping off one head, two more seem to grow in its place, and the monster

will not be laid low until some medical Hercules pierces the heart of it with the shining sword of understanding.

I do not pretend to be such a warrior, but I do feel that glaucoma, or at any rate simple non-inflammatory glaucoma, may indeed be a more simple process than it is now the fashion to believe; that it may, after all, fundamentally be one disease and not many.

There is one division that I would retain, however, and that is the division of all glaucoma, from whatever cause, into inflammatory congestive glaucoma and simple non-inflammatory glaucoma.

This may seem a rather obvious statement, but for all that it is my impression that many discussions as to the cause of glaucoma are confused by failure to keep clear the distinction between two clinically different pathological processes.

The reason I would retain the distinction between the two is this: that though both inflammatory congestive glaucoma and simple non-inflammatory glaucoma are forms of ocular œdema, in congestive glaucoma a venous stasis would appear to be the precipitating cause of the œdematous state, whereas in non-inflammatory glaucoma the arterio-venous factor does not present itself, in my opinion, as any more than, at most, a subsidiary factor.

I know that groups of glaucoma patients have been found to exhibit a degree of vascular instability greater than that found in control groups of non-glaucomatous patients, but it may be that this vasomotor instability is sometimes not the cause but the result of this relentless disease of the sight, with its concomitant anxiety symptoms. Also, in some of these investigations, the difference between congestive and non-inflammatory glaucoma has not been kept in mind. All of us are familiar with the part played by emotion in inducing attacks of acute congestive glaucoma; this is indeed an example of general vasomotor instability acting locally upon the eye, but who can produce irrefutable evidence of the influence of emotion upon the production of simple non-inflammatory glaucoma?

I am venturing to suggest in this paper that despite the conception of glaucoma as a disease of the person and of the personality, despite the modern view of it as another example of psychosomatic disease, simple non-inflammatory glaucoma does not fit in with these conceptions to the same extent as does acute congestive glaucoma. I am venturing to suggest that the dominant factor in the production of non-inflammatory glaucoma is simple interference with the drainage system of the intraocular fluids.

My reasons for putting forward these suggestions are based upon my investigations over the past eight years into a type of simple non-inflammatory glaucoma due to concussional trauma; and upon this subject I have written two papers for the Ophthalmological Society of Australia, entitled "Chronic Monocular Traumatic Glaucoma", "Concussion Glaucoma", and another paper on "Concussion Glaucoma", amplifying these views, shortly to be published in *The British Journal of Ophthalmology*, in London, so you will be mercifully spared the somewhat lengthy details of these investigations, based as they are upon a not inconsiderable number of cases, both from my own practice and from the kindly contributed records of my colleagues.

The inference from this series of cases is this, that if so simple a lesion as concussional trauma can initiate a chronic glaucomatous process, it may be that a simple chronic glaucoma may not be so complex a process as we have thought. My own view, arising as it does from this series of cases, is that simple non-inflammatory chronic glaucoma has, as the dominant factor in its ætiology, an impairment in the drainage system in the trabecular meshwork situated in the posterior part of the cornea.

So, to resume discussion of primary simple non-inflammatory glaucoma, I am aware that nothing novel is offered in my trabecular hypothesis, for trabecular sclerosis has been described by many investigators as the cause of deep anterior-chamber, wide-angle glaucoma; my opinion is, however, that both shallow-chamber and deep-chamber chronic glaucoma have, in their genesis, some interference with or deficiency of the trabecular structure or function.

Probably, indeed almost certainly, it is not always a straight-forward fibrosis, that is to say, a replacement of the endothelial-lined trabecular channels by connective tissue laid down in reaction to toxic or traumatic factors; other reactions are possible, such as the formation of a glass-membrane cuticular product or a senile degenerative process with the displacement of functional tissues by an accumulation of elastic tissue, such as is found in old age in any part of the body's connective tissue strata.

Also, it would be foolish to ignore the role played by other factors in the production of glaucoma; physico-chemical, psychological, vasomotor and autonomic factors have been demonstrated by many workers in many lands. The point is: what is the dominant factor in the initiation of simple non-inflammatory glaucoma, which is the subject of this essay?

It is contended that as simple glaucoma, looked at broadly, is recognized as non-inflammatory and non-congestive, it is illogical to postulate vascular factors, whether of nervous or other origin, as primary factors. In those cases in which a final congestive state develops, these vascular factors must be given their proper place, but many simple cases of glaucoma remain non-inflammatory, even unto the bitter end.

It is often profitable to look back to the earlier observers. In this matter the view held by the pioneers was that the angle of the anterior chamber became obstructed, narrowed or occluded; we now know, thanks to improved microscopic technique and to the invention of the gonioscope, that the angle of the anterior chamber may be open in some cases of glaucoma and not blocked at all. But even the gonioscope cannot demonstrate the presence or absence of trabecular sclerosis.

In some of the cases in my concussion series the patients had deep anterior chambers, some had shallow ones; the latter I assume to be often more in the nature of a terminal condition, for in most cases of chronic glaucoma peripheral synechiæ develop eventually, whatever the original depth of the anterior chambers.

It thus may be that, although the earlier observers were in error in attributing all glaucoma to a closed anterior-chamber angle, and ignorant though they were of the complex vasomotor factors in the precipitation of congestive glaucoma, they were not so much in error in attributing the initiation of simple chronic glaucoma to local mechanical obstruction.

It is my opinion that the vasomotor and nervous factors are merely contributing or precipitating factors and do not play a very significant role in simple glaucoma, unless in an eye already predisposed to glaucoma by impairment of the trabecular filtering structure.

What then does initiate a simple chronic glaucomatous process?

On the hypothesis put forward in this paper, any factor damaging the exit network of the aqueous fluid may initiate such a process, and in consideration of the subject at this stage of the argument, the word "primary" will be discarded, for in the last analysis even "primary" glaucoma must be secondary to some predisposing factor.

To put the matter under headings, the hypothesis is that the predisposing causes are all forms of impairment of the exit mechanism, and that all other causes are merely contributing or precipitating factors.

Predisposing Causes of Simple Non-Inflammatory Glaucoma.

Predisposing causes of simple non-inflammatory glaucoma are (i) hereditary inefficiency of the drainage mechanism; (ii) general (systemic) toxic or metabolic disturbance causing direct damage, by toxic products, to the trabecular meshwork; (iii) toxic changes in the composition of the aqueous fluid, which itself then causes toxic damage to the endothelial network; (iv) direct infection affecting the filtration area; (v) senile tissue degeneration in the trabeculum; (vi) concussional trauma, causing damage either by compression of the corneal trabeculum or by force transmitted through the suddenly compressed aqueous fluid.

The varieties of damage or "changes" mentioned under the above six headings are envisaged as being of two main types: firstly, as a chronic sclerosing or fibrotic lesion, with the formation of connective or cicatricial tissue and the deposition of pigment granules; secondly, as a proliferative process with the development of a cuticular product or "glass membrane" in the trabecular channels.

Contributing Causes of Simple Non-Inflammatory Glaucoma.

Contributing causes of simple non-inflammatory glaucoma are: (i) a shallow anterior-chamber angle, especially in a hypermetrope with a lens relatively large from birth and growing larger as age advances; (ii) any cause of swelling of the lens, especially Morgagnian cataract; (iii) psychological factors, especially the vasomotor instability of the so-called sympatheticotonic individual, with periodic variations in his vascular tone and recurrent partial venous stasis, although it is emphasized that this cause is considered of greater importance in acute congestive glaucoma, or in those cases of simple non-inflammatory glaucoma which pass into a terminal congestive phase, than in those cases which remain non-inflammatory; (iv) autonomic and central nervous system imbalance (apart from psychological causes) with an accompanying upset of the axon reflex system.

Envoy.

Yet, when all that I would say has been said, when my hypothesis has been in all sincerity argued, when a case has been put forward for a mechanical interpretation of the chronic glaucomatous process, there still remains in my mind, as in the minds of all honest men, a sense of mystery and frustration, a sensibility of our limitations and shortcomings, and a realization that we still await the coming of some mental giant who will, in his strength, gather together and coordinate all our small endeavours.

Poets from time immemorial have sung of the beauty of the human eye. They have sung of the soft lustre in the eyes of love, of the flashing eyes of the warrior, of the terrified stare of fear, of the poet's eye "in fine frenzy rolling", of the bright eyes of youth and of the rheumy eyes of crabbed age. They have told us of sad eyes, happy eyes, far-seeing eyes, peering eyes, frank eyes and shifty eyes.

What may we learn from this? True poets are people of intellectual and spiritual vision; they are the seers. Let us then consider carefully on what they say, lest having eyes we see not, neither understand.

Surely, when we come to analyse their observations, we must recognize that what they feel is that the eyes express the individuality of the mind which looks out through them upon the outside world.

We have our backs to the wall; we can ameliorate, but we cannot cure. It is of no use to stand, a bottle of eserine in one hand, a trephine in the other, and like King Canute bid the glaucomatous tide recede. But if we could learn to know when the tide would come in and where the tide would come in, we could tell each other how to avoid it.

For many years I have felt that there may be a glaucomatous type, a glaucomatous diathesis not explicable wholly by local peculiarities of structure or by local anomalies of physiology. Why do some people get glaucoma and why do others live a long and strenuous life immune from it, despite hardening arteries, high blood pressure and disorders of the body fluids? I have put forward some suggestions as to the mechanism of simple non-inflammatory glaucoma; I have, to the best of my ability, shown that such a process may be initiated by the secondary instrument of trauma.

For all that, and as we all know, it is primary glaucoma that comes like a thief in the dark and steals away the unpriced heritage of sight.

So, in the interests of research, and in a spirit of adventure, I will put aside for a while my own mechanistic arguments and postulate a glaucomatous type of personality.

Of what feature might this type be? To me, despite exceptions and variations, it is a gaunt man (or woman) of middle to advanced age; his expression is rather set and sometimes stern, sometimes resigned, hardly ever mobile or frankly happy. To return for an instant to my poets, perhaps the best description of the type I have in mind is Shakespeare's line describing "the lean and hungry Cassius".

These are the lineaments and features of the intense type, one whose emotions are strong but repressed, an introverted personality, no matter what his intellectual ability or lack of ability; they are the characteristics of a personality that uses much mental energy even in the ordinary affairs of everyday life, of one who draws upon his nervous system's reserves excessively and especially upon the reserves of his sympathetic nervous system; in other words, a sympathicotonic type.

If these observations have any truth in them, then what is there about the sympathicotonic individual that may predispose him to glaucoma? Firstly, consider general causes. It is well known that worry, mental stress, may precipitate an attack of acute glaucoma or aggravate chronic glaucoma into becoming acute or subacute. In the sympathicotonic individual we have the chronic worrier; life itself worries him more than it does a more normal person. He is in a constant state of nervous tension.

Now consider local effects. What is the result upon the eye of stimulation of the sympathetic? One result, at least, is stimulation of the *dilator iridis* muscle and enlargement of the pupil. Here then we have one effect which might lead to glaucoma if sustained over a long period: a very slight, hardly noticeable dilatation of the pupil. Of itself it might hardly be considered sufficient impediment to the patency of the angle of the anterior chamber, but further considerations lend some weight to this possibility. For example, what is the normal state of the pupil?

There is considerable evidence that the normal state of the resting pupil is one of contraction. Indeed, Argyll-Robertson thought so, as pointed out by Kevin O'Day of Melbourne, though the idea has to some extent been lost sight of.

In sleep the pupils are contracted, and the deeper the sleep the stronger is the contraction. In the Argyll-Robertson pupil we have a contracted pupil which does not react to light but does react to the stimulus of convergence accommodation. The discoverer of this phenomenon explained it on the hypothesis that it was the *dilator pupillæ* whose tone accounted for the normal light reflex, that the sphincter acted only when the action of light caused the dilator to relax, and that in the particular miosis he observed, the effects were due to paralysis of the sympathetic supply to the *dilator pupillæ*.

Eserine, by inhibiting the destruction of acetylcholine, allows the unstriated muscle of the sphincter to maintain its natural position of contraction, just as it assumes this state during sleep when the dilator's tone is relaxed by virtue of the diminished activity of the sympathetic nervous system.

O'Day points out, in support of this point of view, that there is some embryological evidence for the dilator's being the active factor in light reflex, as only the anterior group of its cells become transformed into muscle tissue. He says:

> It thus bears a remarkable resemblance to the pigment epithelium of the retina, of which layer in actual fact, it is the forward continuation. Although it has never been proved in man, it is known that in lower animals the cells of the pigment epithelium of the retina send processes inwards between the outer members of the rods and cones. Under the influence of light the processes elongate inwards and in the dark contract outwards. The muscle fibres of the dilator are nothing more than the processes of the cells of the anterior of the two posterior layers of the epithelium of the iris and their action is exactly the same as that of the processes of the retinal epithelium. In the light they elongate, and in the dark they contract. The comparison may seem fanciful. It is nevertheless striking. The semi-embryonic state of development of the dilator

would also explain why the pupil will contract to light after all central connections have been destroyed. Although this primitive action is commonly attributed to the sphincter, it seems more probable that it might be retained by the more primitive dilator, the cells retaining their property of responding directly to a light stimulus.

Argyll-Robertson's own explanation of his sign is a much simpler one than those involving some lesion of the afferent path as well as of the sympathetic supply to the dilator.

If this theory, subsequently independently put forward by Uriarte, is correct, and it is hard to refute in view of its applicability to pupillary phenomena, then we have a strengthening of the argument in favour of the postulation of our glaucomatous type. For in the sympathicotonic we may now see a type in which the pupil but rarely attains a fully restful contraction. If it is normal for the pupil to contract when at rest, it is abnormal for it not so to contract.

Of course, it has to be admitted that not all sympathicotonics contract glaucoma, just as all hypermetropes do not contract glaucoma, and that all glaucoma patients are not of a hypertonic nature.

Given, however, a hypermetrope with a lens relatively large from the start of life and growing larger as age advances, given any known or as yet unknown local anatomical or physiological fault in the drainage mechanism of an eye, then add to this a sympathicotonic nervous system, which is unrestful both in the general psychological sense and also in the local sense of inadequate constriction of the resting pupil, and surely we have a symptom-complex worthy of proof or disproof in the clinic and the laboratory.

There is, of course, only the one answer to any theory of cause and effect in medicine, and that is the answer of clinical evidence. I should like to see every case of primary glaucoma investigated by a team.

I should like to have, firstly, the evidence of the general practitioner, the family doctor, for from him could be learnt the patient's mode of life and thought in the past, his general health and its fluctuations, his resistance both to disease and to "the slings and arrows of outrageous fortune".

Secondly, I should like the evidence of the psychiatrist, for he could tell us of the presence or absence of anxiety states in our patient. Even in a more or less amateur way, I have collected many histories from glaucoma patients, of worries and fears and needless obsessions; my evidence as to these things, I realize, is not expert and I should like to have this expert evidence. In some patients I myself have found no trace of these symptoms, but again, just as I have found a preponderance of the sympathicotonic type, so have I found such symptoms present in the great majority of all patients suffering from chronic primary glaucoma.

Thirdly, I should like the evidence of the consulting physician as to the character and type of the patient's metabolic processes, his renal efficiency, his basal metabolic rate and the condition of his whole blood-vascular mechanism. Also I should like to know the response to treatment, if such was necessary, of the patient's nervous system by means of sedatives.

In private practice it is not practicable to have all one's glaucoma patients investigated by a team, yet it is only by having them all investigated that any deductions can be made.

Finally, only by such a pooling of material can anything be done to show whether there are any grains of truth in this bagful of theory, but there is still the evidence we all can use, the evidence of our own eyes. Look at your glaucoma patient not merely as a man with a disease but as a diseased man, and say to yourself: "What manner of man is this?"

It may be that you will see what I have seen, it may well be that you will not; at least you will be looking for something, and what you find may be infinitely more than I have found. You may find that I am wrong; that matters little, for you may find that which you seek.

A BRIEF REVIEW OF INDUSTRIAL DERMATOSES IN WESTERN AUSTRALIA.[1]

By J. M. O'DONNELL,
Perth.

WESTERN AUSTRALIA is not so highly industrialized as other States in Australia, consequently the incidence of industrial skin disease is less than in the eastern States.

Figures taken from the principal insurance office here show that skin diseases represent not more than 1% of industrial accidents. A fair proportion of skin diseases which are compensated are not primarily industrial. These cases are admitted on the score of aggravation by irritants contacted at work. Some of such cases are originally cases of dysidrosis (endogenous), seasonal allergy *et cetera*. Again, a certain number of cases are xerodermatous and the individuals affected should never have gone into industries which involve contact with irritating dusts, liquids or fumes. When I see a child with xeroderma, I always warn the parents against letting the boy take up work such as plastering, cement work and so on.

Infected abrasions with secondary skin sepsis account for a fair number of compensation cases. Harsh cleansers account for a lot more.

One has to remember that repeated attacks of dermatitis caused by contact with an irritant can lead to polysensitization and to chronic skin invalidism. Therefore, if a man has contracted dermatitis in an industry, he should, if possible, be removed from that industry in order to avoid chronic dermatitis. Old patches of dermatitis often recur as the result of contact with new irritants or as the result of working under very hot or wet conditions. This is often seen in cases of dermatitis of the hands and is illustrated in cases of so-called "khaki" dermatitis, in which the old areas and the sites of strong reactions to patch tests break down again in hot weather.

An attack of dermatitis leaves behind it, at times, areas of lowered resistance and skin inferiority at the sites of previous trouble. Generally speaking, the *Workers' Compensation Act* in Western Australia is liberal in that regard and reasonable claims are not often contested. In all cases the patient must be given the benefit of the doubt.

Domestic and Wet Work.

Harsh cleansers, abrasives, soap powders and soap, polishes, vegetable juices, and wet work generally, cause a lot of dermatitis, perionychia and sepsis.

Most of the cases I see are in the older age groups, amongst laundresses, charwomen and housewives. I do not very often see dermatitis in young girls. In this younger age group quite a number of the subjects have a mild degree of xeroderma. Bartenders suffer from septic and monilial perionychia, which is often attributed to dirty swabs. Girls in "pot" bars are more affected, and one often gets a number of cases among girls coming from the same bar; perhaps swabs act as carriers. The new non-drip foot-pedalled tap should lessen the incidence of occupational diseases.

Soda fountain workers get perionychia, dermatitis and skin sepsis from wetness, syrups, sugar *et cetera*. In right-handed people the left hand is more likely to be affected and vice versa. Nail polishes, orange sticks and polish removers may be factors in causation of perionychia.

Rural Industries.

In rural industry all sorts of sensitization dermatitis occur. Many of the cases arise in the July, August, September period, being due to dandelion, capeweed, clover and so on; in the summer months, stinkwort, wheat pollen, grasses *et cetera* cause irritation.

Verrucose pyogenic ulceration occurs fairly frequently as a complication of infected abrasions. My impression is

[1] Read at a meeting of the Section of Dermatology and Industrial Medicine, Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1948.

that this type of septic ulceration occurs more frequently in the dairying districts. I recall one case in which we isolated the tubercle bacillus, although the appearance was that of a typical pyogenic lesion. No fungus has been identified in the lesions. Milker's nodes (vaccinia) occur at times.

Pediculoides ventricosus is also a cause of trouble. We had quite a lot of bother with it during the war period. The palliasses were infested and were referred to by the troops as "itch bags". The method recommended for delousing was the pumping of carbon bisulphide under a tarpaulin covering the palliasses. Men working on ships and railway trucks also become affected when handling infested straw bags *et cetera*.

Keratoses and malignant conditions of the skin produced by exposure to sun and wind are very common, especially in the north and north-west of the State, but are not compensable.

Fertilizers and wheat-pickling mixtures (copper and mercury) also cause dermatitis, as well as nicotine and arsenic in sheep dips.

Mining.

The coal mines are mostly wet, and dermatitis of the feet and legs is quite common. Tinea of the feet has been more common in post-war years than it used to be, possibly owing to the number of infected ex-servicemen returning to the mines. One of the coal mines is putting in new bathrooms with hot water pipes running through the concrete floor to try to keep it dry and so to lessen the incidence of tinea. Varicose veins are also a factor in causation. The water in some of the mines contains mineral and this gives rise to what the men refer to as "salt water boils". In some of the cases the condition is actually seasonal allergic dermatitis *et cetera*, but the men get compensation because of the aggravating effect of the water. Other men break out in dermatitis as the result of working in new drives in the mines where the ventilation is not good. Men working on machines get dermatitis from cleansers, such as harsh soaps, "Dieseline", kerosene *et cetera*.

In the gold mining industry, cleansers such as those mentioned cause dermatitis. Also, men who come in contact with the cyanide plant get dermatitis on the exposed parts; the dermatitis is thought to be due to the alkali rather than to the cyanide. The gold-bearing ore is treated with a solution of potassium cyanide; this forms a slime, which is then run onto zinc shavings, where it concentrates, and contact with the slime or the cyanide on the zinc causes dermatitis.

Arsenic.

At Wiluna, which is a hot place, there is an arsenic refinery where dermatitis and arsenical poisoning occur. Most of the cases I have seen came from the packing room where the white arsenic is put into drums. There are fewer cases now than there used to be, because of the fact that there are not now so many men employed, and because the men are more careful in handling the arsenic and report any symptoms earlier. Respirators are not used by the men, as they found that if the whole of the head was covered breathing became difficult, and also because they developed irritation on the face where the respirator came in contact with the skin—a form of rubber sensitization. They prefer to use a cotton-wool mask, which is about six inches by three inches in size. It is covered with gauze, which is tied round the head. In addition to the cotton-wool mask they put a plug of cotton wool in each nostril. If the mask gets soiled in any way it is discarded at once. The company supplies each man with a fresh set of underwear and overalls each shift. If the men feel any irritation they are encouraged to take a hot bath at once and to don fresh underwear. In the early stages the men were supplied with silk bloomers in an attempt to prevent the irritation and pustular folliculitis of the groins. More recently they have been wearing cotton pyjama pants instead of the bloomers. The overalls go from neck to ankle.

The areas affected by the arsenic are the exposed parts and the nasal septum, conjunctivæ, groins and armpits. The armpits and groins are usually affected with pustular folliculitis and dermatitis. I recall one case in which a careless worker developed a perforated septum in less than a fortnight.

There have been cases of malingering in this industry; the men kept their symptoms going by taking white arsenic by mouth. These cases were detected by carrying out urinalysis from time to time; in several cases we found more arsenic in the urine some months after they had been under treatment with sodium thiosulphate *et cetera* than there had been at the commencement of treatment. That was a pretty sure indication that the men were ingesting arsenic. I recall one case in which a man took so much arsenic in one dose that he collapsed. When his gastric contents were examined it was found that he had had enough arsenic in him to kill a dozen men. In addition to taking arsenic he was also rubbing in sulphur ointment to produce a dermatitis. He took the large dose of arsenic several days before he was going to be examined by a medical referee, who naturally would get a specimen of urine for an arsenic test. Normally urine contains arsenic to the amount of 1:3,000,000. Sectional analysis of hair was also carried out in several cases.

The use of BAL should do much to lessen the deleterious effects of arsenic in those who suffer from any form of such toxæmia. The careless worker in the industry is just begging for trouble.

Engineering Workshops.

Dermatitis is produced by cutting solutions, which are a mixture of mineral oil, soap shavings and water. There was a fair amount of dermatitis in the munition factories during the war, due to these solutions. In one place the number of cases diminished when neat's-foot oil was used in the mixture instead of mineral oil.

Harsh soaps containing abrasives and crude soft soap also caused dermatitis on the hands. Kerosene and "Dieseline", used to remove grease, had the same effect.

Some cutting solutions contain sulphur products, which enhance the cutting qualities of the solution. This sulphur content is also thought to be a factor in producing dermatitis. Spitting into the cutting solution increases the risk of sepsis. Metal filings or "slivers" in the oil also cause infected punctures. The use of sulphonated oil, instead of other more drastic cleansers, has enabled some of my patients with dermatitis to carry on.

Cement and Plaster Industries.

The cement and plaster industries account for a fair number of cases of dermatitis, especially when the worker has a dry skin and is xerodermatous. Minor injuries are notoriously subject to become infected in the presence of lime and cement. Ichthyotics should avoid these industries.

Fellmongering Industry.

In wool scouring, tanning *et cetera*, the hides handled at times have been treated with anti-weavil preparations which contain arsenic. These cause irritation on the hands of those handling the hides. Skins such as kangaroo skins for export have sometimes been so treated.

The majority of cases of dermatitis that I have seen arise in connexion with the unhairing process. Most depilatory mixtures contain slaked lime and sodium sulphide. Men handling pelts which contain these chemicals sometimes get dermatitis on the hands. The "pullers", or men who rub the hair or wool off the skin manually, get septic dermatitis at times.

In tanneries chromates cause dermatitis and ulcers. In wool scouring the alkalis and other fat extractors and solvents cause trouble.

Match Making.

The match head of safety matches contains potassium chlorate and the striking surface of the box contains red phosphorus and phosphorus sulphide. The striking-surface mixture appears to be the cause of skin irritation when the operative accidentally gets soiled with the paste. This is a fairly rare accident under modern working conditions.

Chemical Industry.

In the chemical industry essences, perfumes, menthol, thymol, sandalwood oil *et cetera* are made. One sees a number of cases of dermatitis in men who are sensitive to these various products. If the operatives get their hands soiled they wash vigorously. Several cases recently seen were due to over-use of soap rather than to the chemicals, fumes, extracts *et cetera* with which the individuals had come in contact.

Timber Industry.

In the timber industry dermatitis is caused by jarrah sap amongst the tree fellers and by jarrah sap in green timber handled; also by various chemicals used to preserve the timber against borers and white ants. These preservers at times contain arsenic, which causes dermatitis amongst those handling such wood. In the mill sensitization to various timber dusts occurs.

Canning Industry.

Carrots are heated before being peeled and sectioned. Those handling the hot carrots get dermatitis, some from an actual sensitization, others because of the fact that the process is a wet, hot one.

In the fruit-canning industry perionychia and dermatitis occur. In the apple-canning industry perionychia occurs from the handling of the sectioned apples and from syrups, sugar *et cetera*.

Shoe and Slipper Making.

In shoe and slipper making, sensitization to the dye in various coloured felt occurs, as also to the black and tan dyes used in leather shoes.

Tent Making.

During tent making, irritation round the nostrils occurs from dust caused by high-speed sewing machines working on canvas which has been treated with copper to protect it against tropical moulds. Conjunctivitis also occurs.

The following is an extract from a letter received from the Dux Chemical Solutions Company Limited, of England.

> This Company was the originator of Cupra-Ammonium Processes in dealing with cotton Ducks and probably knows more about this preparation than any other firm in existence. In regard to trouble being experienced in the manufacture of tentage out of Cupra-Ammonium treated Duck, we wish to advise as follows:
>
> The trouble is not due to fumes, but to the fact that the hard Cupric Cellulose Hydroxide finish is fractured when sewing with high production machines, causing an extremely fine, hard dust to come away from the needle holes. This dust forms very minute sharp irregular shaped particles which have an irritating effect (which is purely physical) on the mucous membranes of the operatives. There is no danger whatever in the chemical sense.
>
> The antidote is to bathe the affected parts with milk AND TO OCCASIONALLY SIP MILK TO CLEAR THE THROAT. After a few days the operatives become immune to the irritant dust, and little trouble is then experienced. This is a very old problem which frequently occurs when high production methods of sewing are employed, and has been investigated from the medical point of view.

NON-ECZEMATOUS INDUSTRIAL DERMATITIS.[1]

By J. SUMMONS,
Melbourne.

THE term "industrial dermatitis" immediately conjures up an eczematous reaction of the areas of the skin which are exposed to some industrial irritant. I feel that at this gathering we should have a wider conception of the condition than that defined by the *Workers' Compensation Act* as "a dermatitis due to contact with an irritant of animal, vegetable or mineral origin". This wider conception immediately brings us up against the meaning of the term "industrial dermatitis". Andrews gives the terms "occupational dermatitis", "industrial dermatitis" and "trade eczema" as synonyms, thus showing that he takes the term in its limited sense. This limited type of occupational skin affection is being dealt with by others and, in the short time available, I would like to consider some of the group termed by Prosser White "the dermatogoses". This group, while including the common exudative types of dermatitis, includes many other conditions which can be shown to be without doubt an occupational inflammation of the skin.

It is difficult to arrange a classification of these conditions, but they fall into several main groups.

First and, in Australia, foremost, we have the effects of electromagnetic radiation. As is well-known, the skin response varies with the wave-length of the radiation. Because of this it is convenient to subdivide the group into three main divisions, namely, the effects of ultra-violet irradiation, of infra-red irradiation, and of the irradiation from radium and X-ray machines. It is evident that exposure to such irradiation in the course of work can cause skin damage.

Taking the subdivisions in order, I will first consider solar dermatitis, both acute and chronic. The acute form is obviously a possible form of industrial dermatitis, but the dermatologist is rarely, if ever, consulted, and further discussion is unnecessary.

Now chronic solar dermatitis is a very real problem for outdoor workers in their later years. It seems strange that the opinion of the dermatologist is not more frequently sought to determine if such a condition is occupational. Possibly this is because such dermatitis occurs generally in fishermen and farmers, who are not ardent unionists and so have not got a militant secretary to urge claims. True, quite a number of men in late middle age show a few keratoses, even though their work has always been indoors. The decision as to what constitutes occupational chronic solar dermatitis is far from easy, and in making it the dermatologist would have to draw to a very large extent on judgement and experience. The differentiation between squamous and basal-celled lesions of occupational origin and those occurring from other causes is also difficult, and for this reason I have rather laboured the term "chronic solar dermatitis", which, to me, means that atrophy, pigmentation and solar keratoses must be present on the exposed areas at one and the same time as any carcinoma.

There must be many a man in Australia receiving treatment for chronic solar dermatitis and its sequelæ, for which either he himself is paying or he is receiving charity, when the condition is occupational and, in the case of an employee, should be treated at the cost of the insurance companies. In relation to this, one must be alert to the possibilities that such dermatitis may occur on unexpected areas as a result of specific occupations—for example, the case of the fisherman who developed chronic solar dermatitis on the dorsal surfaces of his feet as a result of the habit of not wearing shoes or socks whilst on the job. Other examples are the recorded cases of alpine guides who showed the effects of reflected ultra-violet irradiation on the submental skin.

One other trap is the case of the arc welder, who is exposed to intense ultra-violet sources and may show the effects as an occupational disease, although his employment has always been indoors.

Passing onto the next subgroup of irradiation effects, one must consider the possible cosmetic effects of prolonged exposure to infra-red rays. A case comes to mind of a ship's fireman who had a bizarre pigmentation of the *erythema ab igne* type over the front of the chest and neck. Although there was no physical disability, the constant jibing by his fellow firemen was having a most unfortunate effect on his mental outlook.

The third and final subgroup includes the effects of radium and X-ray machines. Although these are becoming rare as an occupational condition, a case of a nurse-assistant rather close to home forcibly reminds me that

[1] Read at a meeting of the Section of Dermatology and Industrial Medicine, Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1948.

radiodermatitis is an occupational hazard. Here it is well to remember the possibility of skin damage by the β and γ radiations from radioactive isotopes, which would seem to be coming into general therapeutic and investigational use. With regard to these isotopes, it is interesting to note that, while most disintegrate rapidly, C^{14}, a radioactive isotope of carbon, has a half-life period of more than ten thousand years, and contamination of a building with it necessitates demolition of the building for the workers' safety, not merely closure for a few days or weeks.

Another important and disabling group amongst the dermatogoses are the affections of the nails, mainly onycholysis and perionychia.

The former is frequently seen in washerwomen and others doing a lot of wet work in which trauma is applied to a nail which already has a sodden and damaged nail bed. In this country women are nearly always affected, but in fur-producing countries the process of "fleshing" the furs, that is, separating the dermis from the epidermis, causes a seasonal epidemic of loosening of the nails in men.

The multiple perionychiæ seen in the food-canning industry are worthy of comment. It seems that there is more than the wetness involved as an ætiological factor. The condition is much more common in those processes in which there is the addition of caustic soda to the washing water to facilitate the peeling of the fruit or vegetables. The caustic soda has a softening action on the keratin of the cuticle and makes possible penetration by both bacteria and yeasts. In passing it is interesting that, other factors being equal, women seem more susceptible than men to perionychiæ.

Finally, I should like to review briefly occupational inflammation of the skin due to parasites. No purpose would be served by considering at length all the mites which could be encountered in various types of work, so long as we remember that they constitute a definite occupational hazard and may have far-reaching implications, as was the case in Melbourne when the waterfront was almost tied up as the result of the presence of the causal mite of grain itch in a wheat cargo.

The lower parasites must also be remembered when we are dealing with cases of animal ringworm in such people as farmers, grooms and kennelmen.

In this brief résumé of certain inflammations, neither treatment nor prevention has been mentioned, and the whole purpose of the paper has been to call to mind certain conditions which at times seem to be in danger of becoming lost in the mass of literature which appears on the exudative forms of industrial dermatitis. It behoves us as medical men to remember the possibility of forms of dermatitis of occupational origin which do not fall within the legal definition of this condition.

RECENT EXPERIENCES IN LONDON ON THE USE OF PHYSICAL MEDICINE IN ARTHRITIS.

By JOHN A. SHANASY,
Brisbane.

As the care of the sick and injured in England is gradully becoming departmentalized, a medical metamorphosis is already obvious. Many patients from almost all departments of hospitals require physical therapy, occupational therapy *et cetera*, consequently the new social concept has enormously increased the importance of physical medicine departments. The majority of patients observed in these departments belonged to the rheumatic and orthopædic groups, although many were referred from other sections of hospitals.

Rheumatic diseases, which include all types annotated in the Royal College of Physicians' classification, are grouped in special clinics and treated with great advantage by rheumatologists. Of the rheumatic group a large number is being treated at the Charterhouse Rheumatism Clinic with a minimum of physical therapy. Treatment in difficult cases here relies substantially on the laboratory guidance of Dr. Harry Coke. His tests for metabolic dysfunction and endocrine factors, and his comprehensive interpretation of the differential sedimentation test will be the subject of a future paper.

Another school of thought in the rheumatic group is in Manchester. At Ancoat's Hospital, Manchester, Dr. A. Renshaw, basing his treatment on post-mortem findings in the intestinal mucosa of chronic arthritics, advises no physical therapy and permits none other than very mild faradism and galvanism. A preparation of Bengers, Limited, containing erepsin, and presented under the name of "Benecol", is administered by mouth. X-ray therapy had not been given in conjunction with this product in cases of ankylosing spondylitis.[1]

At the Royal Red Cross Rheumatism Clinic at Peto Place there are all the advantages of a spa in London. In addition to the usual light, electrotherapy *et cetera* there is the only really extensive balneotherapy department in the city. On the staff of Peto Place are such well-known authorities as Dr. M. B. Ray, Dr. F. Howitt, Dr. C. B. Heald, Dr. W. S. C. Copeman, to mention but a few, and it is the work here and at such institutions as the Royal Free Hospital, Saint Stephen's Hospital and Saint Thomas's Hospital that will be of greatest interest.

London has a variety of apparatus not in general use in Australia, such as the "Bertholet" cabinet for convenient steam vapour treatment of legs and arms, the "Studa" chair for colon lavage, which requires a certain amount of muscular effort by the patient, and the "Guthrie-Smith" bed. This useful apparatus has had notable additions made by Dr. Heald—namely, a hydraulic stretcher support, and chains for speedy adjustments instead of ropes.

Basic Factors in Physical Medicine.

The frequently repeated dogma that physical medicine employs the basic factors of Nature's forces—sun, water, heat, cold, electricity *et cetera*—for the maintenance and restoration of function is generally accepted. It is on and through that very complex structure the skin that the effect is produced. Heat, massage and physical and electrical methods can cause increased circulation and similar effect, and the method used depends on the facilities at one's disposal.

The application of the numerous methods in physical medicine departments at the various hospitals shows little variation and conforms to well-known and accepted principles.

Organization.

At Saint Thomas's Hospital the physical medicine department is under a medical supervisor whose duty is (i) to correlate the work from all other departments, (ii) to direct the staff, and (iii) to see that the department is not a dumping ground for incurables. His staff includes physiotherapists, almoners, and instructors in games and gymnastics, education, crafts and occupational therapy. He arranges domestic tests in houses adjacent to rehabilitation centres, and cooperation with other departments including pensions and labour officials.

A physiotherapist accompanies each patient to the medical officer responsible, sees the patient examined, hears the diagnosis, and receives direct instructions. First a definite clinical diagnosis is arrived at, then it is decided what type or combination of types of physiotherapy is most suitable, then (i) the strength, (ii) the duration and (iii) the extent and frequency of application are definitely prescribed. When possible a target is indicated to the physiotherapist; for example, in a case of disseminated sclerosis, instead of instructing the physiotherapist to institute coordinating exercises, the directions should be "Train this patient to walk" or "Train this patient to feed herself in one month's time". At the next visit to the medical officer the physiotherapist again accompanies the patient for computation of results and further instructions.

Arthritis.

Treatment of arthritis depends on the type and stage of the disease, on the general condition of the patient and on many other factors. In physical medicine departments

all methods are used, including rest only, with orthopædic aids, electrotherapy, light and hydrotherapy, heat and cold, mechanotherapy, occupational therapy, X-ray treatment, massage and manipulation. The application depends on the indications presented by the patient under treatment.

Psychological, environmental, infective, endocrine, metabolic, dietetic, constitutional, occupational and all miscellaneous factors receive due consideration and appropriate treatment. It is important to remember that in rheumatic diseases physical medicine is an adjunct only to treatment.

The tendency in gold treatment is to give injections on a lower dosage scale than previously. Toxic sequelæ are few and results are better. There has been no investigation into the use of the sulphonamide group of drugs to parallel that of Parr and Shipton.[3]

Injection Treatment of Joints.

The injection treatment of osteoarthritic joints has had a long and varied trial. Other forms of arthritis, including rheumatoid arthritis and ankylosing spondylitis, have also received intraarticular and/or periarticular injection treatment, but the method is not generally practised outside the osteoarthritic group.

An X-ray examination is essential before a decision in favour of injection is made, for a reasonable amount of joint space must be demonstrated.

Some authorities follow their injections with a moderate amount of manipulation and non-weight-bearing exercises. Others prescribe a few days' rest after injection; nevertheless it was noticed that many of the latter patients walked home. Many are the preparations used for joint injections. Despite the variety of preparations injected and the differences in after-treatment, all workers claim good results. Good results are gauged by prolonged symptomatic relief of pain, improved mobility and improved ambulatory function.

Those who believe that the pain in osteoarthritic joints is due to the concomitant synovitis must visualize an improvement in the pathological state after a series of injections, at least so far as the synovitis is concerned, for the symptomatic relief and improvement in joint function far outlive the immediate effect of a series of injections. One exponent of the method has by serial X-ray films demonstrated an increase in joint space.

It was interesting to note that some always inject procaine into adjacent fibrositic nodules when these are present before injecting the joint. These nodules always follow the pattern first described by Stockman and Renton, of Glasgow,[3] and more recently elaborated by Kellgren,[4] Kelly[5] and others. This additional procedure is an improvement in technique.

The following preparations are used: procaine (0·5% to 2% solution); lactic acid with procaine (Waugh) prepared by Brady and Martin; acid potassium phosphate and acid magnesium phosphate (Coke) prepared by Allen and Hanbury, Limited; benzyl salicylate (10%) in oil (Copeman) prepared by Martindale; "Gomenoleo" (Laughton Scott) prepared by *Laboratoires des Produits de Gomenol, Paris*; lipiodol (Fletcher), a Lafay preparation.

Fletcher in a small series of cases demonstrated a high percentage of good results with lipiodol injections into osteoarthritic knee joints; but the immediate reaction is severe and painful.[6] Crowe claims that the results with acid potassium phosphate and acid magnesium phosphate are superior to those obtained with all other preparations. He states that the addition of procaine is unnecessary,[7] but it was noticed that this was a usual and considerate addition. Reactions following acid magnesium phosphate are sometimes severe, but severe reactions are unusual after the injection of acid potassium phosphate. Both these solutions are declared by Allen and Hanbury, Limited, to remain stable indefinitely.

The most generally used preparation is W. Grant Waugh's lactic acid procaine solution,[8] manufactured by Brady and Martin of Newcastle-on-Tyne. Unfortunately this preparation, issued with a pH of 5·8, deteriorates on the sea journey to Australia. I brought out three samples; one was kept at a constant temperature of 16° F., another at 38° F., and a third at cabin temperature. The sample kept at 16° F. had a pH of 5·1 when tested at the University of Adelaide. The pH of the others was well below 5·0. Brady and Martin advise that their preparation should not be used when the pH drops below 5·2. This buffered solution is now satisfactorily prepared by several Australian manufacturers.

Hip Joint Injections.—With regard to hip joint injections, authorities differ as to the better method of approach. Crowe declares the anterior approach to have many advantages. Waugh, Heald and others adopt the lateral approach. Actually both are simple when use is made of the skiagram as the main guide, and due attention is paid to anatomical variations. Immediately after the injection, moderate traction, manipulation and non-weight-bearing exercises on the Guthrie-Smith apparatus are instituted. Flexion and extension, abduction and adduction, and circumduction are each performed for ten minutes. Improvised non-weight-bearing exercises, including cycling, are recommended for home treatment. On the surgical side, osteoarthritic hips are being treated by vitallium cup insertion, nail arthrodesis, obturator nerve section combined with adductor tenotomy for contracture, and other surgical procedures. The fact that there is so much divergence of opinion concerning (i) the choice of preparation for injection, (ii) the after-treatment, (iii) the technique of injection, and (iv) other procedures, including surgery, does not necessarily imply that any of these methods are based on false premises. All have been well tried. All give good results in carefully selected cases. A necessary background to the treatment of arthritis is a sound knowledge of each method, in order that the particular procedure most likely to be of greatest benefit in each case may be predetermined.

The Importance of the Almoner.

On the economic side, the almoner's function is a minor one. Her chief duty is to know the home and working conditions, living costs *et cetera*—that is, the background particularly relevant to the condition—and to pass on the information to the medical officer and be the link between hospital, family and friendly societies. To this may be added a link with the employment exchange and the employer, for until disablement rehabilitation officers gain more experience this link is substantially the almoner.

When the time comes to estimate the fitness of an arthritic, for example, for his previous occupation or for lighter work, the almoner obtains the information concerning the lighter work that is available. When a satisfactory occupation is decided on, to make him fit for that particular work becomes the target of the physical medicine department. About two weeks before his discharge the almoner notifies the employment exchange, the disablement rehabilitation officer approaches the almoner, and the numerous forms inseparable from government control are completed.

The aim throughout treatment is to make fit an arthritic or other disabled person for a full-time, fully paid, suitable job, and to place him in that job. Progress reports are subsequently presented to the medical officer by the almoner after the patient's return to work.

Practical Implications.

All the largest factories in England employ a percentage of disabled persons in appropriate occupations at full wages. Physical medicine departments are of paramount importance in the implementation of this system. In addition, the British Government is at present organizing "disabled persons' corporations".

Except for the lamentable shortage of beds, particularly for rheumatic patients, hospital facilities and medical attention in Australia are of exceptionally high standard; but there is a tendency to allow disabled persons to lapse into the physical and psychological frustration of permanent pensioners, when more could be done to train them for suitable fully paid occupations.

An interesting development in organization was started in the Royal Air Force during the war and is now firmly

established at the Royal Free Hospital, London. Three sections, (i) rheumatology, (ii) orthopædics, and (iii) physical medicine, are closely associated under the name of the medical rehabilitation unit. This medical rehabilitation unit has evolved successful cooperation between the three sections and is worthy of consideration as a set-up in organization in Australia.

Kovács's quotation[9] of Morton Smart's summing up of the position in Britain can well be applied, with little adjustment, to Australia.

The Commonwealth Government is now pledged to a great increase in the facilities for medical and surgical treatment of all individuals. It should enlist the advice of the Australian Association of Physical Medicine in order to establish a comprehensive national scheme of physical medicine, with well-organized industrial clinics to supply the needs outside of hospitals.

Acknowledgements.

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STREPTOMYCIN IN PULMONARY TUBERCULOSIS: A REVIEW OF SIX CASES.

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PREVIOUS to 1940 a great number of agents had been tried to combat tuberculosis. These included the heavy metals, dyes and sulphonamides. However, the most significant attempt at rational chemotherapy has been the introduction of the antibiotics in the field of treatment of this disease. These comprise streptomycin, subtilin, and fungus and lichen extractions. Also related to this category may be the various synthetic chemicals now being investigated, such as 5-amino-2-butoxy-pyridine, *p*-amino salicylic acid, the phenothiazines *et cetera*, which appear to be relatively less toxic.

Streptomycin is produced by *Actinomyces griseus* and was first reported by Waksman in 1944. Since then an intensive campaign investigating its properties and actions has been carried out by numerous workers. It has been standardized in terms of weight of pure substance, one microgramme of the streptomycin base being approximately equivalent to the original "S" unit, which was defined as "that amount which would inhibit the growth of a particular strain of *Entamœba coli* in 1 c.c. of nutrient broth". Thus its dosage in relation to tuberculosis is purely empirical.

Still very little is known of the mechanism of action of streptomycin; even the question whether it has a bacteriostatic or bactericidal action *in vivo* is not definitely answered. It cannot be administered orally, as it is not adequately absorbed in the gastro-intestinal tract. The intravenous route appears to enhance the toxicity of the drug. Thus the intramuscular and intrathecal routes are the two best.

Since the inception of treatment with the drug the dosages administered have become smaller. Toxic effects have been reported in a high percentage of cases by most workers using 1·8 grammes or more daily. These have included the following: (i) local reactions, (ii) sensitivity with rash formation, (iii) urinary casts and albuminuria, (iv) symptoms of vestibular impairment. However, with the smaller dosages now recommended, these have been reduced to a small percentage.

The resistance to the drug of certain strains of the tubercle bacillus after some weeks of therapy has also been described.

General investigations have shown that streptomycin is efficacious in only certain types of tuberculosis; ulcerative, miliary and meningeal lesions, and those pulmonary lesions which are of an early productive and exudative type and which have not yet caseated, show the readiest response. Streptomycin is highly basic, highly water-soluble and highly ionized, and the slightly acid and high lipoid and enzyme properties of caseous tissue appear to prevent streptomycin from reaching the tubercle bacillus in sufficient concentration to combat effectively this type of the disease.

The first six patients treated for pulmonary tuberculosis with streptomycin following a period of bed rest in this hospital have been selected for review; they are four females and two males with an average age of thirty years.

Owing to the changing information in current medical literature, three different forms of dosage were applied: in the first case 0·25 gramme was administered four times a day; this was followed by 0·5 gramme twice a day and then by 0·5 gramme once a day. All these doses were given by the intramuscular route (in one millilitre of saline solution) and for periods varying from two to three months, 45 grammes being the maximum total amount given to any one patient.

The types of lesions chosen for this therapy were all progressive and mainly exudative in character, unilateral or bilateral cavitation being present in each instance. In all cases the sputum contained tubercle bacilli and the blood sedimentation rate was increased. The common clinical features were: (i) the presence of cough and sputum, (ii) loss of appetite and loss in weight, (iii) evening pyrexia, (iv) lethargy and dyspnœa. In three of these cases artificial pneumothorax had been attempted and failed. Two of the patients had bilateral lesions and one was treated before thoracoplasty to prevent spreading of a new lesion.

Results.

The general results were as follows.

Clinical Observations.

The cough and sputum decreased almost immediately in all cases. The appetite and weight improved steadily in all cases. Before therapy the temperature was recorded as between 99° and 103° F., and in all cases this had returned to normal or almost normal limits within eight days. One patient on a three months' régime developed a recurrent pyrexia two months after the commencement of treatment. The main obvious effect throughout was the remarkable immediate improvement in general appearance and the feeling of well-being; patients who had been lethargic and dyspnœic became vital and composed.

Laboratory Observations.

The blood sedimentation rate improved greatly in one case, improved slightly in two cases, remained stationary in two cases, and became slightly worse in one case. In

all cases except one, the sputum continued to contain tubercle bacilli, the one exception being the case in which thoracoplasty was performed. The urinary findings remained unaltered.

Radiological Observations.

In all cases, prior to treatment, pulmonary cavitation and infiltration existed. During and after therapy, X-ray pictures in no case showed improvement. In two cases the cavities increased in size. In one case an extension to the contralateral lung occurred.

Toxicity.

There were no local reactions. A non-irritative, maculopapular rash appeared on the trunk and face in one case on the tenth day after the commencement of therapy and disappeared during treatment fifteen days later. No albuminuria occurred. With regard to possible vestibular impairment, the caloric stimulation test failed to reveal absence or diminution of response. There was no tinnitus or impaired hearing, no blurring of vision and no ataxia.

Discussion.

The most obvious effect of streptomycin therapy has been the rapid clinical improvement in all patients—this, despite the fact that the X-ray appearances of their lungs, the results of sputum tests for tubercle bacilli, and the blood sedimentation rates all remained relatively uninfluenced by the drug.

There was also a relative absence of toxic manifestation.

This is only a small series of cases, but they vary somewhat from those previously reported in association with streptomycin therapy, as only clinical improvement has been shown. The drug appears in this series to have had no effect on the macroscopic tuberculous lesions.

The mode of action of streptomycin would appear to have been one of the following: (i) the production of a microscopic absorption of exudate; (ii) the action on a superimposed secondary infection; (iii) the action on a possible toxin liberated by the tubercle bacillus itself.

Summary.

1. Six patients suffering from pulmonary tuberculosis have been treated with varying doses of streptomycin.

2. An identical course in the disease was produced in each case.

3. Improvement occurred clinically in each case, but other factors appeared uninfluenced.

4. The subsequent progress of these patients is being followed.

Acknowledgement.

I wish to express thanks to Dr. D. R. W. Cowan, physician in charge of the Chest Clinic and of Frome Ward at the Royal Adelaide Hospital, for his advice and his permission to publish these cases.

THE ROYAL PRINCE ALFRED HOSPITAL CANCER OF THE UTERUS FOLLOW-UP.

By HERBERT H. SCHLINK, CLEMENT L. CHAPMAN and FREDERICK N. CHENHALL,

From the King George V Memorial Hospital for Mothers and Babies, Sydney.

THE uterine cancer register of our unit was closed on December 31, 1948, so that we are now in a position to publish the five and ten year results of treatment for the years 1930 to 1943 inclusive. The results are set out in the accompanying tables.

Cancer of Cervix Uteri.

Up till the present there have been two unit teams working in the King George V Hospital within the Royal Prince Alfred Hospital, and each adopted slightly different methods of approach to treatment. Quite recently a third gynæcological surgeon was appointed and fortunately all three teams have now agreed to carry out as a routine the combined method of treatment which has proved so successful in our hands. The figures recorded here are those of our team, but with the reorganized staff adopting a uniform method of treatment they will be greatly augmented and of greater interest in future years.

Since our last published results (THE MEDICAL JOURNAL OF AUSTRALIA, September 18, 1948, page 317) we have made no alteration in our method of pre-operative radium application. We still advise one application of 7000 milligrammes of radium, prior to operation or to any further treatment by radiotherapy, and thereby differ from the Swedish school, which divides the dosage and does not have recourse to subsequent surgery. Our technique is as follows: 30 milligrammes of radium with platinum screenage of one millimetre are applied to the full length of the uterus and two corks of 20 milligrammes of radium with two millimetres of platinum are applied to the lateral fornices; all radium is removed after 100 hours. Thus 7000 milligramme-hours of radium treatment are given. From four to six weeks later a radical hysterectomy of the Wertheim type with removal of the lymph gland areas is performed.

We have further evidence of the non-effectiveness of radiotherapy on lymph glands when attacked by squamous or adenocarcinomatous cancer cells.

Our operability rate has remained at about 50% of all patients seen and the lymph gland involvement in the patients operated on at about 25%.

TABLE I.

Five and Ten Year Absolute Cure and Survival Rates of Cancer of Cervix Uteri, 1930–1943, the Royal Prince Alfred Hospital. Compiled December 31, 1948.

Observation.	Observed Five Years. Number or Percentage Rate.	Observed Ten Years. Number or Percentage Rate.
All patients seen and examined with a view to treatment	499	300
Patients treated[1]: all diagnoses microscopically proved	479	291
Alive without recurrence	152	78
Alive with recurrence	8	2
Died of cancer	303	200
Died of intercurrent disease	10	8
Lost or not followed up	6	3
Cure rate amongst all patients seen	30·5%	26·0%
Survival rate amongst all patients seen	32·1%	26·7%
Cure rate amongst all patients treated	31·1%	26·8%
Survival rate amongst all patients treated	33·4%	27·5%

[1] Mortality in radical Wertheim's panhysterectomy for cancer of *cervix uteri*; 367 performed with 18 deaths = 4·9%. There have been no post-operative deaths since 1945.

We still have little faith in deep X-ray therapy for cervical cancer and fail to see the logic of Taussig's operation of lymphadenectomy with conservation of radiotherapeutically treated uteri when the devitalized and usually senile organs (which might still contain embalmed living cancer cells) can be removed with their lymph draining areas by the radical Wertheim hysterectomy without any greater surgical risk.

Our figures for cancer of the cervix after excluding stage IV patients and those dying from intercurrent disease remain about the same.

We are pleased to note that Alexander Brunschwig of Cornell University, New York, has had the courage to commence the surgical treatment in the stage IV cases and in those cases in which all other forms of treatment, whether radiological or otherwise, have failed to cure or palliate the pain and distress which accompany the final stages of this disease. All cancer workers who have had to stand by and watch these hopeless patients slowly perish in intolerable pain and agony must acclaim and encourage this humane and palliative treatment, however radical it might appear to be. We congratulate Mr. Brunschwig on his low overall post-operative mortality of 5·5%.

In the King George V Hospital within the Royal Prince Alfred only the patients in stages I, II and III are surgically treated, and the average operative mortality of all surgeons performing the radical Wertheim hysterectomy is 4·9%, but as all gain more dexterity it is believed that it will be reduced still further.

In our unit no post-operative death has occurred since 1945, probably owing to the more frequent use of blood transfusions and the help of chemotherapy.

TABLE IIA.

Carcinoma of Cervix. Five Year Relative Survival Rates, 1930–1943, Royal Prince Alfred Hospital. Compiled December 31, 1948.

Technique.	Stage I.		Stage II.		Stage III.		Stage IV.		Total.		
	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Percentage.
Radium *plus* surgery ..	37	25	99	55	96	43	—	—	232	123	52·6
Radium	3	2	31	10	133	21	70	4	237	37	15·6
Nil or incomplete treatment	—	—	—	—	11	—	19	—	30	—	—
Total	40	27	130	65	240	64	89	4	499	160	32·1

TABLE IIB.

Carcinoma of Cervix. Ten Year Relative Survival Rates, 1930–1943, Royal Prince Alfred Hospital. Compiled December 31, 1948.

Technique.	Stage I.		Stage II.		Stage III.		Stage IV.		Total.		
	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Percentage.
Radium *plus* surgery ..	21	13	59	31	50	21	—	—	130	65	50·0
Radium	2	1	13	4	95	8	45	2	155	15	9·0
Nil or incomplete treatment	—	—	—	—	4	—	11	—	15	—	—
Total	23	14	72	35	149	29	56	2	300	80	26·7

Morbidity following operation has been no greater than that following other major pelvic operations. After 367 radical Wertheim hysterectomies 18 patients died, 19 suffered from one or other of the following immediate post-operative complications: thrombosis, embolism, pneumonia, pyelonephritis or fistula. Three hundred and thirty had normal convalescences. Fourteen developed remote complications, mostly fistula, resulting from the radium or a recurrence of the growth. One patient developed stenosis of both ureters with pyelonephritis four and three-quarter years after radium application.

TABLE III.

Survival Rate Excluding Group IV and Deaths from Intercurrent Disease, all Lost Cases Assumed to be Dead, Compiled December 31, 1948.

Treatment.	Excluding Group IV.		Excluding Both Group IV and Intercurrent Disease Deaths.	
	Five Years.	Ten Years.	Five Years.	Ten Years.
A. Radium *plus* surgery ..	52·6%	50·0%	54·7%	53·1%
B. Radium alone	19·8%	11·8%	21·4%	12·2%
C. Average of A and B ..	39·1%	33·3%	43·4%	34·5%

As stated by all workers interested in this subject, the only prospect of improving five and ten year results lies in: (*a*) The awakening of women to present themselves on the first signs of abnormal bleeding or discharge. (*b*) The education of all practitioners to recognize the disease early. (*c*) The sending of patients with diagnosed and doubtful lesions to established cancer clinics where teams consisting of surgeons, radiotherapeutists, pathologists *et cetera* are competent to advise what form of treatment should be adopted. Surgically the assistants of such a clinic should be as efficient as the operator himself in all details concerning operative procedure. (*d*) The establishment of preventive cancer clinics and the universal use of the Papanicolaou test as an adjunct to biopsy.

Cancer of Corpus Uteri.

The follow-up of our *corpus uteri* cancers has been improved and will soon be as thorough as that of our cervical cancers.

TABLE IV.

Carcinoma of the Corpus Uteri. Five and Ten Years Survival Rate, 1930–1943, Royal Prince Alfred Hospital.

Observation.	Five Years.	Ten Years.
Patients examined with a view to treatment	91	50
Patients treated	88	48
Alive	54	17
Died of cancer	30	23
Died of intercurrent disease	1	5
Lost or not followed up	3	3
Survival rate amongst all patients seen ..	59·3%	34·0%
Survival rate amongst all patients treated ..	61·4%	35·4%

TABLE V.

Carcinoma of the Corpus Uteri, 1930–1943, Royal Prince Alfred Hospital.

Treatment.	Number of Cases.	Alive.
Five year survival:		
Radium *plus* surgery or surgery alone	70	50
Radium alone	18	4
Nil or incomplete surgery	3	—
Total	91	54
Ten year survival:		
Radium *plus* surgery or surgery alone	38	17
Radium alone	10	—
Nil or incomplete surgery	2	—
Total	50	17

Acknowledgements.

We wish to thank Dr. Frank Pigott, the Joseph Foreman Fellow in Gynæcology, who has prepared these statistics and by his own personal energy discovered many lost patients; the Commissioner of Police and the Registrar-General for their help in untraced patients; our pathologists, Dr. Geoffrey Davies and Dr. Mary Heseltine, and their assistants; Miss Cunningham and our personal secretaries, as well as our nursing and operating staffs for their tenacious efforts in keeping these statistics up to date. All do this beyond-the-clock work for the information of the profession and public in an entirely honorary capacity.

Reports of Cases.

MORBILLI BULLOSI.

By S. E. J. ROBERTSON, M.B., B.S., M.R.A.C.P.,
Sydney.

THE appearance of pemphigoid elements in the exanthem of measles is of sufficient rarity to justify the recording of any cases that appear. Ronaldson (1937), after a study of the literature, divided the reported cases into three types: (*a*) cases in which a bullous eruption was associated with a morbilliform erythema; (*b*) cases of measles in which a bullous eruption followed the true rash, either immediately or after a varying interval; (*c*) cases of well authenticated measles with an eruption which had pemphigoid elements.

Most of the reported cases fell into the first category and were probably cases of acute pemphigus associated with a morbilliform rash. The evidence of measles in this group is very scanty and the recording of a catarrhal onset with Koplik spots and the appearance of measles in susceptible contacts is lacking. Acute pemphigus usually manifests itself by bullæ on the otherwise unaffected skin and on the buccal mucous membrane and is not accompanied by catarrhal conjunctivitis and bronchitis.

In the second category are those cases in which a pemphigoid eruption occurs at some time after the acute stage and may follow scarlet fever, whooping cough and varicella, as well as measles. These cases are again probably pemphigus occurring on skin debilitated by illness (Ronaldson, 1937).

Cases in the third category are true *morbilli bullosi*. This is not a separate variety of measles, but it occurs when the causative virus assumes such virulence that the exudative reaction in the deeper layers of the skin is intense enough to cause bullæ to form on the rash. At the same time there is a corresponding increase in the severity of the infection in the upper and lower parts of the respiratory tract, the conjunctivæ and the mouth, and the general condition becomes grave. Ronaldson (1937) quotes two cases of this type, in one of which the patient recovered, out of 4362 cases of measles. He records eosinopenia as being of importance in distinguishing the condition from acute pemphigus. Neff (1920), whose fatal case is the only one in the literature of the United States, believed that he was dealing with a distinct disease complicating measles because of the occurrence of leucocytosis. However, the presence of bronchopneumonia could account for this finding, and he was probably dealing with *morbilli bullosi*. Morton (1921) reported an apparently typical fatal case, but doubt must be thrown on the diagnosis because of the history of a previous attack of measles, the non-observance of Koplik spots and the failure of a susceptible contact to develop measles.

James and Miller (1938) reported another fatal case, in which they found what may have been inclusion bodies in cells in a centrifuged specimen of bullous fluid. They believe that, including their own case, only five cases had been reported in the literature. The following is thought to be the sixth.

Clinical Record.

V.O., a female, aged four years, had very fair hair and fine, pale skin. She was found to have a small area of pneumonia at the base of the lower lobe of the left lung on July 31, 1948. She was put to bed at home and treated with sulphadiazine, 0·64 gramme every four hours, and alkalis. On August 3 her temperature was normal and no abnormal signs were detected in her lungs. Sulphadiazine was continued for a further forty-eight hours.

On August 5 her temperature suddenly rose to 101° F. On examination, she had conjunctival injection, nasal discharge, faucial inflammation and Koplik spots. Owing to the recent lung infection sulphadiazine was continued as a prophylactic measure. Pink macules were observed behind the ears and the hair margin of the forehead on the following day. A fusing rash of red maculo-papules with clear areas of skin between, typical of measles, appeared on August 7, and laryngo-bronchitis developed. During the following four days the rash became thicker, but, apart from conjunctivitis more severe than usual, the illness was an ordinary severe attack of measles. On August 12, the child was drowsy, her pulse rate was 140 per minute and her temperature 102° F. The rash was dull red in colour, raised and velvety-looking, and confluent on the face. Dull red patches were noticed on the soft palate. It was considered that the child was suffering from the toxic variety of measles as mentioned by Harries and Mitman (1947). The child was gravely ill on August 13, her pulse rate was 160 per minute and her temperature was 103° F. The rash was confluent on many areas of the chest and abdomen, the eyes were tightly closed with a thin mucous discharge, a severe aphthous stomatitis possibly due to monilia had developed, the fauces were very red and swollen, and numerous moderately crepitant râles were heard over both lungs. On this, the seventh day of the exanthem, bullæ first appeared. They commenced on the face, on that portion of the rash which was most acute, and contained fluid which was slightly cloudy. Each bulla reached its maximum size of about four centimetres in diameter in eight hours and then ruptured leaving a raw area. At first it was thought that they might have been due to sulphadiazine and this was suspended. However, further bullæ appeared for three more days on the face, lips, neck, trunk and arms, and the rash became confluent over the whole body surface. The child remained gravely ill with a continuous temperature in the vicinity of 103° F., severe conjunctivitis, stomatitis and bronchitis. On August 17 no further bullæ appeared, the temperature began to fall by lysis and the rash began to fade. Desquamation commenced on the following day and involved the entire body surface in the ensuing week. The temperature became normal on August 21. Cough and signs of bronchitis persisted for another four weeks, since when the child has been very well. No special methods of treatment were used other than those used in any case of severe measles. Precautions against secondary infection were carefully carried out, and only the mother and medical attendant, heavily masked, entered the sick room. On August 20 the sister, the only susceptible contact, developed conjunctivitis, nasal catarrh and Koplik spots, followed by a typical morbilliform eruption two days later and a moderately severe attack of measles.

Comment.

There can be no doubt that this child had measles of a very severe type. It is unnecessary to explain the bullæ by supposing that a second infection, acute pemphigus, was coexistent. The question will be raised as to whether the bullæ could have been due to sulphadiazine intoxication. Cases of a pemphigoid eruption have been reported following the sulphonamides. Shaffer *et alii* (1943) mention bullæ on the otherwise unaffected skin following the giving of sulphathiazole; they recurred immediately after further administration. Patch testing was not performed. Peterkin (1945) saw one bullous eruption amongst 500 sulphonamide rashes following sulphathiazole administration. Only bullous elements were present on the skin and patch testing is not mentioned. Cole (1946) describes three cases with the same features. No other cases could be found in the literature.

In an attempt to determine if any sensitivity was present, one of the original tablets used was powdered, mixed with petroleum jelly, and applied to the skin of the patient as a patch. No reaction was observed after forty-eight and ninety-six hours. However, sulphadiazine sensitivity can be excluded on clinical grounds. The signs which became worse during the bullous eruption were those of any severe measles infection as it affects the eyes, skin and respiratory tract, and these are not seen in sulphonamide toxicity. The bullæ at no time appeared in any area where the morbilliform rash was not at its worst. The signs became worse after use of the drug ceased and did not begin to abate till four days later.

Summary.

In most reports of *morbilli bullosi* the evidence of measles is scanty or absent. A case of *morbilli bullosi* is described. Sulphonamide sensitivity is excluded.

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CHRONIC NEPHRITIS IN A CHILD OF TWELVE.

By GEOFFREY SERPELL,
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CHRONIC NEPHRITIS in children is not a common disease. The following case is of interest because of the marked fibrosis of the kidneys and consequent great reduction in size found at autopsy, the short duration of the illness, the only one from which the child had suffered, and the absence of a history of any illness which could be incriminated as responsible for the chronic nephritis found at post-mortem examination.

Clinical History.

J.W., aged twelve years, was admitted to hospital with the history that until five days previously he had been quite well. At this time he noticed weakness of the legs and felt generally "off colour". He was taken to see his local doctor who at that stage could find nothing definitely the matter with him. Since then his parents noticed that he was becoming more drowsy and that he vomited everything eaten. On the day of his admission to hospital he had been suffering from repeated nose bleeding. The only other abnormality that had been observed by his parents was that whereas in previous years at school he had been very bright, this year he had failed in all subjects.

There was nothing significant in the family history, and the child had had no previous serious illnesses.

On examination, the boy was semi-comatose and pale, with sunken eyes, and there was blood about the nostrils. His temperature was subnormal and pulse rate was 88 per minute. Examination of the lungs, heart, abdomen and nervous system revealed no abnormality. A moderate amount of albumin was found to be present in the urine, and blood only was withdrawn on lumbar puncture. The blood pressure, unfortunately, was not recorded.

A few hours after his admission to hospital the child died.

Post-Mortem Examination.

At autopsy the body was found to be that of a poorly developed young boy. No lesion was found in the heart, liver, spleen or gastro-intestinal tract. The lungs were congested and consolidated at the bases on both sides. The brain was found to be generally œdematous, but no other structural change was observed.

The left kidney, which at first could not be found, weighed two pennyweights and was about one centimetre in diameter. It was at first thought to be a lymph gland, but section revealed tissue resembling renal cortex. This was confirmed microscopically.

The right kidney was subnormal in size weighing three ounces. It had a scarred surface with firmly adherent capsule. Section of the kidney revealed a normal medulla and blood vessels, but the cortex showed much scarring.

Histopathology.

The report on the microscopic examination of a section of the kidney was as follows:

> The small fragment of renal tissue shows considerable alteration in normal structure. Only about a dozen glomeruli are present. A few are healthy and fairly large. Some show partial hyalinization with adhesion of the tufts to the capsule. One or two show extremely thickened hyaline Bowman's capsules and one or two completely hyaline. The tubules are sometimes small and atrophic, sometimes distended, and contain colloid casts. There seems to be some hypertrophy of convoluted tubules. There is a general increase in fibrosis, more marked in some parts than in others, and some round cell infiltration. The larger vessels have quite thick walls. The smaller arterioles are not so severely affected. Comment: The appearances are the end result of long continued damage, the thickened Bowman's capsules suggesting that ischæmic processes have played the greater part, at least in recent years.

Discussion.

As with any other pathological process, so with chronic nephritis, it must be defined in terms of space and time, and thus a definite functional disturbance corresponding to a particular morbid anatomical picture can be stated. Chronic nephritis, or more accurately "chronic renal damage", may be defined as the end result of one of several disease processes acting over a long period of time on the kidney and characterized functionally by renal insufficiency, and structurally by marked fibrosis, retrogressive vascular changes and retrogressive or inflammatory changes in the nephron. The time factor in the definition must be stressed. Chronic nephritis is the end result of the action over a long period of time of one of several pathological processes.

The several pathological processes are the following: (*a*) Bacterial infections, as in pyelonephritis, syphilis *et cetera*; (*b*) bacterial allergy, as in glomerulonephritis (probably); (*c*) vascular disease, as in benign and malignant hypertension, "arteriosclerotic kidney" of the aged, and *periarteritis nodosa*; (*d*) toxic action, as in lead poisioning and toxæmia of pregnancy; (*e*) metabolic disturbances, as in gout and *diabetes mellitus*; (*f*) endocrine disorders, as in association with parathyreoid tumours; (*g*) degenerative lesions of the kidney, as in "nephrosis" and amyloidosis. Of these, the most important with regard to the ætiology of chronic nephritis in children, are glomerulonephritis, pyelonephritis, vascular disease and lead poisoning.

Chronic nephritis in children has been classified by Sinn into three groups, as follows: Group 1: Associated with congenital abnormality of the urinary tract, for example, hypoplasia of the kidney, hydronephrosis, hydroureter *et cetera*. In this group are also included cases secondary to pyelonephritis, pyelitis *et cetera*, because these usually affect congenitally abnormal kidneys. Group 2: Chronic nephritis as the terminal stage of acute or subacute glomerulonephritis. Group 3: Renal destruction in malignant hypertension.

In a review of seventeen cases of chronic nephritis occurring over a five-year period at the Children's Hospital, Melbourne, Sinn found thirteen cases associated with congenital abnormality of the urinary tract, two occurring as a terminal stage of acute or subacute glomerulonephritis, and two cases in association with malignant hypertension. Thus, congenital abnormality of the urinary tract forms the commonest ætiological background for chronic nephritis in children.

The complete absence of any suggestive history of glomerulonephritis prevents the inclusion of this case in Sinn's Group 2, although it must be borne in mind that latent glomerulonephritis may have been present. The arterial lesions found on microscopic section are not those of malignant hypertension, and coupled with the absence of any suggestive history, exclude the case from Group 3.

It would therefore appear that this case falls into Sinn's Group 1, chronic nephritis associated with congenital urinary tract abnormality. The extremely small left kidney could possibly be hypoplastic, and then secondarily affected by disease, but the evidence is inconclusive and marked fibrosis alone could just as readily be invoked as an explanation for the small size of the kidney.

There is no evidence of glomerulonephritis, and the appearances of the arterial sclerosis and fibrosis of renal stroma are not those of any rapid process such as occurs in malignant hypertension, so the proposition thus presents itself that a relatively slow destruction of renal tissue has occurred during the child's lifetime. The starting point may well have been in the small left kidney which, as has been well shown, could produce secondary hypertension and thus secondary slow damage in the other kidney.

Whether the initial lesion was in the arterial bed or of inflammatory nature involving the glomeruli cannot be ascertained; nor can it be determined whether the disease process commenced during intrauterine life or after birth; and if it commenced after birth whether severe disease produced marked fibrosis of a normal sized organ, or whether inflammation produced further reduction in size of a previously hypoplastic kidney. Fibrotic lesions of the glomerular tufts and thickening of the arterial walls have been demonstrated in the newborn, indicating that similar processes to that seen in later life may take place *in utero*. Renal damage, arterial sclerosis and renal fibrosis may thus commence early in life and may even be congenital.

The assumption that a kidney has not developed normally is implied in the term "congenital hypoplastic kidney". It is now recognized that this term must be used with some caution and understanding, for what is observed to be a very small kidney during later childhood or adult life may be the result, not of a defect of differentiation and growth of genetic origin, but of an unfavourable environmental change *in utero* or early post-natal life.

In the case under discussion, the grossly diseased kidneys with resultant renal insufficiency would explain the poor physical development of the boy and his recent failure at school-work. The pneumonia found at autopsy was a terminal phenomenon. Unfortunately the blood pressure was not recorded, and had it been, this observation might have helped in establishing a diagnosis. Both Sinn and Guild, Kendall and Gibson, in a paper on arteriosclerosis in childhood, stress the importance of recording the blood pressure in the examination of all children, and the error of omission in this case supports their view.

The insidious manner in which chronic nephritis may develop is also well shown, for this child must have had a slowly progressing pathological process affecting his kidneys for several years, and yet during this time he showed no clinically apparent abnormality. Finally, this case demonstrates that in all "diagnostic problems" in children, especially coma and semi-coma, chronic renal disease must be considered.

Summary.

A case of chronic nephritis in a child twelve years of age, with an illness lasting only five days and terminating fatally, together with the post-mortem findings, is recorded.

It is considered that the case was one of vascular disease producing "chronic nephritis" and arguments are put forward that the diagnosis of "congenital hypoplastic kidney" should be made only with reservations as to the possible nature of disease processes of environmental type.

Acknowledgement.

I must thank Dr. J. D. Hicks, pathologist, for his great help in the preparation of this case report, and Dr. Stanley Williams, pædiatrician, Prince Henry's Hospital, Melbourne, for permission to report the case.

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Reviews.

GASTRO-ENTEROLOGY.

"AN INTRODUCTION TO GASTRO-ENTEROLOGY", by Walter C. Alvarez, is now a well-known treatise, which has reached its fourth edition.[1] Alvarez has spent his life studying and recording gastro-intestinal disorders. In this book he has collected a great deal of information for the student and practitioner, much of it theoretical and scientific and a great deal of practical value. In the main, however, he deals with the physiology of the gastro-intestinal tract rather than with the clinical aspects of disease. In this respect the book is certainly introductory and physiological, rather than clinical, though, if it is carefully studied, there are a great many valuable clinical points to be learned from it.

Alvarez appears to direct his attention mainly to what mechanisms cause symptoms of indigestion, and what physiological results follow operations, such as vagotomy and cholecystectomy, rather than to the clinical pictures or the treatment of disease. Thus the book will not have a wide appeal to practitioners who wish to know the diet for patients with ulcers and the like. Alvarez does not appear to be enthusiastic about vagotomy for peptic ulcer, though he states that the operation often relieves pain. The physiological effects of section of vagus nerves are, however, rather serious in many cases, according to his analyses. There is very little in this book about gastroscopy; indeed Alvarez refers students to other books for information about that method of investigation.

For a study of the physiology of the gastro-intestinal tract Alvarez's book is to be recommended, but it scarcely covers the disorders of the gastro-intestinal tract with sufficient relation to the clinical aspects to attract the attention of the general practitioner.

HEARING AND ITS PRESERVATION.

THE author of "Ways to Better Hearing", who has himself a 70% hearing loss, still is active in business and enjoys social intercourse. He has written a book primarily for the layman, in a straightforward and convincing style, on the methods of getting the best use of whatever hearing one has, as well as of preserving and improving whatever function remains in defective ears.[2] One is surprised to learn that one of every seven adults is hard of hearing or actually quite deaf; and that out of the whole school population, 1·5% need special training. Of these unfortunates even in enlightened communities only the most severely affected receive even a small proportion of the care they need. The electric audiometer is the only scientific test of impaired hearing, and the early recognition of poor hearing is difficult. In some cities an enlightened public has established an annual audiometer test for every child. Money spent on the prevention of deafness and the special training and education of children with impaired hearing saves larger sums for the control of the backward and delinquent. The various forms of psychological damage due to defective hearing are clearly described. The reality of the dangers arising from self-deception and self-consciousness in the early stages of deaf-

[1] "An Introduction to Gastro-Enterology", by Walter C. Alvarez; Fourth Edition, revised and enlarged; 1948. New York: Paul B. Hoeber, Incorporated. 10" × 7", pp. 932, with 186 illustrations. Price: $12.50.

[2] "Ways to Better Hearing: A Practical Guide for Anyone with Defective Ears", by Lowell Brentano, with an Introduction by Arthur G. Wells, M.B., B.A., F.R.C.S.; 1948. London: George Allen and Unwin, Limited. 8½" × 5", pp. 214, with a few illustrations. Price: 10s. 6d.

ness is stressed, as is the need for a hearing aid and its skilful use by the sufferer before it is too late. Not only must the hard of hearing face the facts, but also the family and intimates must cooperate to help him make full use of whatever hearing he has. Only too often the family and the medical adviser of the deaf fail him by lack of understanding and consideration. No one ever laughed at a blind man because of the effects of his affliction, but only too often the hard of hearing are unnecessarily made to feel ridiculous or conspicuous.

This book is invaluable to doctors, teachers and welfare workers not only for the sound advice that it gives, but also for the facts set out in a breezy convincing style, and the comprehensive lists of words and sentences to be used as exercises in reeducating the possessor of a hearing aid. Appendices deal with methods of rating hearing aids, and other practical details pertaining to their use.

DRUGS FROM PLANTS.

MANKIND has made use of plants in the treatment of disease for at least four thousand years, and from this has developed much of vital importance in modern medicine. "Drugs from Plants", by T. I. Williams, number ten of "Sigma Introductions to Science", is a little book which tells the fascinating story of the evolution of modern therapeutics.[1]

It begins with a brief history of medicine and herbalism from early Egyptian times, passing thence to Babylon, Greece, Rome, and by way of Arabic medicine to the Middle Ages. Next follows a section on the growth of scientific knowledge of plant products, telling how the active principles have been isolated and in some cases synthesized.

Subsequent chapters tell the story of seven important plant products, quinine, hashish, digitalis, penicillin, ergot, opium and cocaine. These are all interesting, but that on penicillin deserves special mention for its historical survey of antibiotics as well as its account of the discovery and final mass production of penicillin.

On the cover the book is said to be for the general reader, but we fear that much of it will be found too technical by many people. This is a pity, but perhaps those who are shy of technicalities will skip them. James Harvey Robinson remarked that "scientific popularisers are prone to set a poor trap with no bait". Here the bait is mostly good, but at times a little insipid.

"Drugs from Plants" may be recommended to the intelligent general reader, and to medical undergraduates and nurses; but it is feared that the medical student has little time for general interest in his subjects, for he is already overwhelmed by text-books, often "not only too hard, but also too long". The print is good, errors are absent, and errors of fact are few and not important.

HÆMOLYTIC PHENOMENA.

A VALUABLE lesson in the approach to a biological problem is taught by Ponder in his monograph "Hemolysis and Related Phenomena".[2] The modest claim of a guide to the student of hæmolytic phenomena becomes an essay in biophysics which includes information not to be found in texts dealing with the physiology of the red cell, although a more than elementary knowledge of mathematics is necessary for complete appreciation of the information presented.

The stimulating lesson is revealed in the introductory chapter where attention is drawn to the body of theory regarding permeability, volume change, and eventual hæmolysis of the mammalian red cell, that is in many respects a description of "an imaginary situation". This observation is directed against the conception that behaviouristic problems of the red cell can be solved in the light of the permeability theory and a model of a membrane-invested cell.

The chapters on red cell shape where interesting observations are made on the reversibility of disk sphere transformations reveal, as does the whole text, the author's high regard for cytochemistry and cell surface structure. The almost invariable occurrence of these shape alterations as a preliminary to hæmolysis, and the factors such as pH, the type of hæmolysin and the presence of antisphering substance, indicate the numerous influences which remain unaccounted for in fragility tests in clinical practice.

Chapter III includes some observations on hæmatocrit determinations which are pertinent to the loose way in which packed cell volumes are spoken of in clinical practice without regard for the physical details relating to centrifugation, bore of hæmatocrit tube and anticoagulants.

The chapter devoted to cytochemistry and architecture presents a wealth of chemical detail and emphasizes the complex structure of the red cell. A short section on the morphology and development of the red cell, its reaction to dyes and the significance of basophilia is admirably instructive, presenting detail which is lacking in hæmatological texts.

The final chapter on hæmolysis *in vivo* deals fully with hæmolytic systems and their inhibitors. Various clinical hæmolytic syndromes are also discussed. A short note in this section on the Van den Bergh reaction is disappointing in that the author has not dealt with it more fully.

Four appendices, including a section on red cells of lower animals, the technique of red cell counting and the metabolism of the red cell, supply unique information. Attention is especially drawn to the section on red cell counting, where interesting facts are supplied concerning the sources of error in routine methods.

A selective bibliography, familiarity with which is recommended by the author in order to acquire fundamental principles, completes a valuable work essential to the student of red cell behaviour.

A YEAR BOOK OF DERMATOLOGY AND SYPHILOLOGY.

"THE 1948 YEAR BOOK OF DERMATOLOGY AND SYPHILOLOGY" will appeal primarily to the dermatologist, but there is much in it to interest a wider circle of medical readers.[1] Following their usual custom of contributing a special article at the beginning of the book, the editors, Marion B. Sulzberger and Rudolf L. Baer, discuss carefully and at length eczematous eruptions of the hands; general practitioners, as well as dermatologists, would find this worth perusal. The arrangement of the material in the book, which comes from a wide field both medically and geographically, is the same as in the volume for the previous year. The first ten sections are concerned with skin conditions and cover respectively treatment and prevention, X-ray and other physical therapy, eczematous dermatitis and urticaria (allergic and non-allergic), with a subsection on allergy, miscellaneous hæmatogenous dermatoses, other dermatoses, cancers, precanceroses and other tumours, *mycosis fungoides* and leuchæmia, fungous infections, and other infections and infestations. Section 11 deals with venereal diseases (exclusive of gonorrhœa); a large subsection on syphilis, in which modern treatment and some important aspects of diagnosis are discussed, is followed by a shorter section on other venereal diseases. Section 12 is of particular interest. It deals with "Investigative Studies" in two subdivisions respectively on dermatology and venereal diseases, but the material grouped here concerns all those who are, as the editors put it, "interested in the fundamentals of medicine and the basic sciences". The relation of the skin and its responses to the body as a whole, as well as the value of the skin as a test tissue for a great variety of investigations, is well brought out in a large selection of interesting abstracts. This section is the highlight of a volume in which the high standard of previous years is fully maintained.

A TEXT-BOOK OF ANÆSTHETICS.

ROSS AND FAIRLIE would have some difficulty in recognizing the latest edition of their handbook now given the name and stature of a text-book. It has grown considerably in both size and substance and is most attractively presented, its knowledge being offered in a well set out and easily read form. The seventh edition[3] has a number of new plates

[1] "Drugs from Plants", by Trevor Illtyd Williams, B.A., B.Sc., D.Phil.; 1947. London: Sigma Books, Limited. Sydney: Walter Standish and Sons. 7¼" × 5", pp. 120, with illustrations. Price: 6s.

[2] "Hemolysis and Related Phenomena", by Eric Ponder; 1948. London: J. and A. Churchill, Limited. 9" × 6", pp. 416, with 69 illustrations. Price: 50s.

[1] "The 1948 Year Book of Dermatology and Syphilology", edited by Marion B. Sulzberger, M.D., and Rudolf L. Baer, M.D.; 1948. Chicago: The Year Book Publishers Incorporated. 7" × 4¾", pp. 563, with 72 illustrations. Price: $5.00.

[3] "A Textbook of Anæsthetics", by R. J. Minnitt, M.D. (Liverpool), D.A. (R.C.P. and S. Eng.), and John Gillies, M.C., M.B., Ch.B. (Edin.), F.R.C.S. (Edin.), D.A. (Eng.); Seventh Edition; 1948. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5", pp. 568, with illustrations. Price: 30s.

and illustrations which always improve a work of this nature. It might be still further improved by the removal of some of the older pictures which no longer have any but historical value.

One of the best chapters is that devoted to "Posture of the Patient". This is a most important consideration to the whole surgical team and to the patient. It is regrettable that it receives such inadequate attention in most books on anæsthesia. Most of the positions in frequent use are described and pictured, but there are a few omissions. For instance, no mention is made of the lateral or prone positions used for thoracic and cardiac surgery.

The arrival and firm establishment of curare have added a chapter to the book. It covers the history of this much glamorized drug and deals briefly with preparation, pharmacology, methods of administration, contraindications and therapeutic uses, finishing with a solemn warning to the "student" of the dangers attendant upon the use of curare by the uninitiated. The other relaxants receive not even a mention, which may be a wise omission, for some of them have already lost their popularity.

No less than 130 pages out of a total of 550 are devoted to "Regional Analgesia". This is rather more space than usual for this aspect of anæsthesia, but the section is extremely well done and forms a most useful part of the book. The text has been rewritten and is well illustrated. The relevant anatomy is adequately described and details of technique are given with a very pleasing clearness. Mr. Wevill writes this section and he leaves no doubts in the reader's mind that he is conversant with the practical points as well as with the theoretical ones, and is indeed a master of the art. A notable omission from the section, and indeed from most works dealing with local analgesia, is detail relating to the preparation and sterilization of the solutions used and the varying amounts of adrenaline which may be added with safety for use in the different regions.

The paper, type and binding of this edition are excellent. The work is written primarily for students of anæsthesia, and for them it is excellent. A specialist, though still a student, would thoroughly enjoy the presentation and knowledge of this book, but might be a little disappointed that many of the questions he wishes to ask are still unanswered.

HUMANISM AS A PHILOSOPHY.

IN "Humanism as a Philosophy" Dr. Corliss Lamont has attempted to write a handbook on a rounded philosophy of life which can motivate mankind to a millennium.[1] His humanism is based on a naturalistic attitude towards the universe, ruling out all trace of the supernatural. He believes that man is an evolutionary product and has no existence after death. Mankind must solve its own problems in a world in which fatalism and determinism are non-existent. Humanity can find humanism a worthwhile ethic, or morality, based on earthly experience.

The author in the spirit of the knight-errant goes forth to fight the traditional figures of our social order. He has a ready pen and a wide acquaintance with authors new and old. As he modestly writes: "My indebtedness to others approaches infinity."

One of the merits of this book is as a mine of quotations. One has the feeling that at times the authors would be surprised at the purpose to which their brain children have been employed. Buddha, Confucius and the Old Testament Hebrews contribute their quota to humanism. They accompany Fitzgerald:

> Oh, threats of Hell and Hopes of Paradise!
> One thing at least is certain—This Life flies;
> One thing is certain and the rest is lies;
> The Flower that once has blown for ever dies.

And Markham:

> We men of Earth have here the stuff
> Of Paradise—we have enough!
> We need no other stones to build
> The Temple of the Unfulfilled—
> No other ivory for the doors—
> No other marble for the floors—
> No other cedar for the beam
> And dome of man's immortal dream.

The theme that "life is all and enough" takes up the first portion of the book and is followed by one on "Humanism's Theory of the Universe".

Dr. Lamont discusses Hegel, Marx, Schopenhauer and Wordsworth. It becomes increasingly obvious that humanism is a new religion. The author, however, swiftly tugs the reins of his oratorical steed and turns us back into humanism as a philosophy. There is room for neat quibbling on the differences between them.

The final section of the book deals with the "Affirmation of Life". It is less convincing than the earlier pages. The final test of an hypothesis is not one of appearance but of efficiency. In spite of their errors and omissions, the great religions have provided motives and ideals for the millions. They continue to do so. The "humanism" of Dr. Lamont has a woolliness which is unsubstantial. The faith which is worth while dying for must have clear-cut features. Few would give up their lives for a spate of words, however beautiful or well arranged.

The author himself seems to have doubts on this question. He buttresses his faith with a belief in a new social order. It is one with which we are very familiar—a communistic chimera in which the police state is non-existent, but the scene is filled with a gorgeous vision of high ideals and achievements which will end in a classless society.

He deals tenderly with the disciples of Marx and uses the word fascist as synonymous with deviltry. In one delightfully naïve paragraph he infers that all communists are sincere in their intention to bring about an enduring democracy on the principle of all for each and each for all, and must therefore be admitted to the ranks of democratic humanists. On the strength of such entirely unscientific and very partisan reasoning, his plea for the Lamontian type of humanism as a scientific approach to the world's religions and philosophic problems loses its force.

As the scene unfolds, the author touches upon international democracy and leaves us with the comforting thought that when the majority of mankind has acquired the philosophy of humanism, all will be well. It may be incontrovertible that in a community of angels there will be no war, but such unpractical considerations in a world troubled by intrigue surely belong to the realm of academic philosophy.

Much of this book is in the same category and should be judged as an intellectual phantasy rather than as a serious scientific approach to the world's problems. Perhaps at some later date Dr. Lamont may discard his emotional blinkers, throw away his book of quotations and let us see an unobscured vision of reality. Until that occurs the reader is advised to be critical of such wordy propaganda for socialistic theories and stick to his "illusions".

[1] "Humanism as a Philosophy", by Corliss Lamont; 1949. New York: Philosophical Library. 8½" × 5½", pp. 376. Price: $3.75.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Psychological Aspects of Clinical Medicine", by Stephen Barton Hall, M.D., D.P.M.; 1949. London: H. K. Lewis and Company, Limited. 8¼" × 5¼", pp. 432, with six illustrations. Price: 21s.

Based on a course of clinical lectures for final year and post-graduate students at the Liverpool Medical School.

"The 1948 Year Book of Endocrinology, Metabolism and Nutrition"; Endocrinology, edited by Willard O. Thompson, M.D.; Metabolism and Nutrition, edited by Tom D. Spies, M.D.; 1949. Chicago: The Year Book Publishers, Incorporated. 7" × 4½", pp. 546. Price: $4.50.

One of the "Practical Medicine Series of Year Books".

"Clinical Radiation Therapy", by Ira I. Kaplan, M.D., F.A.C.R.; Second Edition; 1949. New York: Paul B. Hoeber, Incorporated. 9¼" × 5¾", pp. 868, with 614 illustrations. Price: $15.00.

Intended to provide for students, practitioners and specialists an answer to problems associated with radiation therapy.

"Histology and Histopathology of the Eye and its Adnexa", by I. G. Sommers, M.D.; 1949. New York: Grune and Stratton. 8¼" × 5¼", pp. 804, with 69 illustrations. Price: $12.00.

An elaboration of lectures given to students.

"Microbiology and Man", by Jorgen Birkeland, Ph.D.; Second Edition; 1949. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 5¾", pp. 544, with 54 illustrations. Price: 37s. 6d.

Designed as an elementary text-book for the student, the book deals with the part played by microorganisms in the environment of man, and it deals with man himself.

The Medical Journal of Australia

SATURDAY, AUGUST 6, 1949.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of apaper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

NEW OPERATIONS FOR THE RELIEF OF MITRAL STENOSIS.

Two new surgical operations for the relief of mitral stenosis have been devised with such brilliance and carried out with such success that it is necessary to examine carefully their background, possibilities and limitations. Mitral valvular stenosis is such a common affection of the heart damaged by rheumatism and so many sufferers from it have heard and remember the name, that the medical profession is certain to be besieged by inquiries about these operations as soon as news of them spreads, as it must, among the public.

The first of the new procedures has been described by C. P. Bailey, Associate Professor of Thoracic Surgery in the Hahnemann Medical College, Philadelphia, and called by him "commissurotomy".[1] Commissurotomy consists in enlarging the orifice of the mitral valve by cutting its commissures with an instrument attached to the surgeon's index finger, introduced through an opening in the auricle of the left atrium. It may be regarded as the perfection, or as a considerable stride towards the perfection, of the operations of valvulotomy, valvulectomy and valvular dilatation that have been devised and tentatively practised in the past. It is nearly fifty years since Sir Lauder Brunton first suggested that mitral stenosis might be surgically cured; it is nearly twenty-five since H. S. Souttar, of London, performed the first successful operation, which consisted of digital dilatation of the mitral orifice by way of the auricle of the left atrium. A few years before Souttar's operation E. C. Cutler and S. A. Levine had cut the stenosed mitral valve with a tenotome without upsetting the patient, but without greatly relieving the obstruction to the flow of blood. Shortly afterwards, in 1923, Evarts A. Graham, of St. Louis, with his collaborator, D. S. Allen, devised a cardioscope, which was introduced into the left atrium through its auricle and lowered till it was in contact with the mitral valve; the valve could then be seen just as one can see one's finger in a glass of milk if one presses it against the inside of the glass. This cardioscope carried a cutting instrument with which the valve could be cut. It was soon concluded, from the researches and further experiences of Cutler, Levine and C. S. Beck, that valvulotomy would not achieve sufficient relief of the stenosis and that some form of partial valvulectomy was to be preferred; but no success was achieved. Valvulectomy produced, of course, a much greater degree of mitral valvular incompetence than previously existed, for which the heart was by no means adapted by its former defect and which it appeared unable to tolerate. The chief lesson learnt from these early essays was that the auricle of the left atrium, which appears to have little physiological function, could endure considerable manipulation without harm to the heart.

After the publication by Cutler and Beck of their final review in 1929 the surgery of the mitral valve seems to have fallen into abeyance until quite lately. The most recent experiments in the relief of mitral stenosis, unpublished but referred to by Bailey, have been the anastomosis of the azygos vein with a pulmonary vein by R. H. Sweet, of Boston, and the production of an artificial aperture in the interatrial septum by Bailey and by D. Harken. These procedures would seem difficult to justify; they reduce pulmonary hypertension to be sure, but they do so at the expense of reducing a cardiac output already barely sufficient, to increase which the whole complex compensatory mechanism of left atrial hypertrophy and pulmonary hypertension has been brought into play. Bailey's own operation is based on the idea that by cutting the commissures of the stenotic mitral valve well out into the tissues of the mitral ring he might possibly allow the two halves to be separated by the current of blood during diastole yet to come together and prevent regurgitation of blood during systole. He states that this idea flowed from the observation that in the stenosed mitral valve the thick fibrotic plaque is surrounded by a margin of fairly normal valvular tissue. He may well have reflected also, though he does not allude to Souttar, that in Souttar's successful operation, accomplished by means of digital dilatation, the dilatation must almost certainly have been effected by a tearing of the tissues at the commissures of the valve. Before putting his idea into practice in the human subject, Bailey performed operations on the mitral valves of some sixty dogs, a method of preparation and a precaution which are usual among American surgeons, but not emulated sufficiently by surgeons in this country. He also had the advantage of correspondence with H. G. Smithy, of Charleston, who has made extensive studies of the means of protecting the heart from arrhythmia, which may cause sudden death during operative interference. Up to the time of reporting Bailey had performed commissurotomy on eight patients: in three cases the operation was successful, one patient died two and a half months after the operation and four died as a result of the intervention. Digitalis and quinidine were administered before the operation and an intravenous injection of procaine was given while it was in progress to prevent arrhythmia. Antibiotics were given to prevent infection of the wound and of the cut valve surfaces. Anticoagulant therapy was thought to be dangerous and unnecessary.

It is worthy of note that the first to rise and congratulate C. P. Bailey when he presented his paper at a medical convention was Evarts A. Graham, that ingenious and universally respected pioneer in the surgery of the mitral valve as in so many other fields of thoracic surgery; his

[1] *Diseases of the Chest*, April, 1949.

language was that of high praise. He was followed by Gordon Murray, of Toronto. Murray in the course of his remarks announced another novel operation for the relief of mitral stenosis, which he has successfully performed. This is to remove the lateral cusp of the stenosed mitral valve with a punch under endoscopic vision and immediately to replace it with an artificial valve. This is made from a section of the cephalic vein, turned inside out so that its intima lies in the blood-stream; it is stiffened and reinforced by a piece of the tendon of the *palmaris longus* muscle and it is inserted from before aft through the heart on the ventricular side of the site of the original valve, so that on systole it is jammed into the opening left by the resection of the valve, while in diastole it floats out of the opening so that it does not obstruct the filling of the ventricle. How it is retained in position was not stated. Murray mentioned that he had carried out extensive animal experiments in the construction and fitting of artificial mitral valves before operating on a human subject. He had operated successfully on two human subjects up to the time of reporting. It appears that he has not tried the effect of metal or plastic valves in the human subject as yet.

Bailey and Murray have builded well on the work of the pioneers and they have striven painstakingly and ingeniously to fit themselves for their extraordinary surgical achievements. These are at once an inspiration for others to follow and to improve and a warning of the disasters that await those who, in their eagerness to alleviate suffering, may be tempted to follow with inadequate self-preparation. Bailey makes the statement that there are at least one million people suffering from mitral stenosis in the United States of America, one-quarter of whom are suitable for surgery. We feel that he may have somewhat overstated the position here, for elsewhere he recommends that his operation should be performed only on persons who no longer suffer from active rheumatism and in whom mitral stenosis is the sole valvular lesion present. Moreover, there must be many of the hypothetical million patients whose mitral stenosis is the sole valvular lesion present but does not impose a serious handicap on the heart; and there must be many more who exhibit obvious physical signs of mitral stenosis but whose chief disability is produced by the incapacity of arteriosclerotic coronary vessels to nourish well an enlarged and damaged heart. The most pressing indication for operation, in Bailey's opinion, is hæmoptysis, especially if it is severe, for of such patients 66% die within three years. It should be borne in mind here that many persons with mitral stenosis who cough up blood are suffering from pulmonary infarction, not from severe obstruction to the flow of blood through the valve. At all events the appearance of these new operations will make necessary a careful and intelligent assessment of the state of the heart of very many persons suffering from valvular disease, and when operative surgery is thought to offer a prospect of relief, exact physiological studies will be desirable. These are very complicated and time-consuming and require the services of highly trained staffs of physicians and biochemists. If we are ever to see good heart surgery in this country and, in particular, if we are to profit from the initiative of Bailey and Murray, we must train physiologists to study the dynamics of the heart, sending them abroad for the purpose, if necessary; we must insist also that our thoracic surgeons have the opportunity to become thoroughly grounded in surgery on the experimental animal.

Current Comment.

STREPTOMYCIN AND CHRONIC BONE INFECTIONS.

CHRONIC OSTEOMYELITIS can be very resistant to treatment and can continue to distress and discourage the patient as well as exasperate his medical attendant, despite all efforts to deal with it. All possible aids are pressed into service. This is one field, however, in which not much has been said about the use of streptomycin, so that it is of interest to find this the subject of a report. It comes from J. C. Wilson,[1] who undertook a clinical study to determine whether or not the systemic and local use of streptomycin, in addition to thorough sequestrectomy and meticulous wound care, would hasten the healing of wounds of patients ill with osteomyelitis of long duration. He presents the results obtained in 25 cases of chronic osteomyelitis, in which discharging sinuses had been present for an average of nineteen months. Many types of treatment had been tried without success. In an effort to promote healing, a plan of therapy was evolved upon the following principles: (i) thorough investigation of the wound bacteria; (ii) radical sequestrectomy after adequate pre-operative preparation; (iii) the administration of streptomycin and penicillin before, during and after surgery; (iv) meticulous wound care after surgery to prevent contamination. Wilson states that 21 patients have responded very favourably to this regimen and their wounds have healed. Four patients failed to respond and all these have had amputations. He strongly emphasizes the point that the use of streptomycin offers no panacea for the treatment of chronic osteomyelitis. The drug is not a replacement for adequate surgery, but, when combined with thorough sequestrectomy, it is beneficial in the promotion of healing. Some details of the scheme of treatment warrant mention. If bacteria were sensitive to 16 microgrammes or less of streptomycin per millilitre of medium, the systemic use of the drug was considered advisable. However, if the sensitivity proved greater than 16, streptomycin was used locally and none was given by the intramuscular route. In addition to streptomycin, penicillin was given intramuscularly in doses varying from 50,000 to 100,000 units every three or four hours, depending upon the severity and the sensitivity of the infection caused by Gram-positive organisms. These appeared often after streptomycin had controlled large numbers of Gram-negative bacteria. Unless toxicity developed, penicillin administration was continued until the wound had healed. After adequate sequestrectomy, which Wilson states is the most important single part of treatment, 200,000 units of penicillin in five millilitres of normal saline were poured into the wound. Streptomycin-plasma mixture was then dusted over the wound surfaces. Next, the wound was lined with glass cloth. This material was chosen as a wound dressing because its fine mesh prevents granulations from growing into the substance of the dressing. Glass cloth is not irritating, it keeps wound surfaces smooth and prevents the growth of ragged, hyperabundant granulations, and at the time of dressing the cloth can be lifted from the wound with ease and with a minimal amount of discomfort to the patient. The glass cloth was packed loosely with dry gauze and a voluminous dressing was applied. Fourteen days after operation, under strict aseptic technique in the operating theatre, the wound was inspected. The glass cloth was lifted gently from the wound and a swab was taken for culture. A layer of fibrin often covered granulations. This was removed, so that the antibiotic drugs could be in more intimate contact with the healing surfaces. Streptomycin in plasma and penicillin were then added and the wound was again

[1] *The Journal of Bone and Joint Surgery*, October, 1948.

dressed with glass cloth. Dressings were subsequently done at weekly intervals in the operating room until the wound had healed or until such a small patch of granulations remained that careful dressing in the ward would not endanger the final healing. Wilson points out that the local use of streptomycin should be continued until the wound heals, for although Gram-negative bacteria may disappear early from culture, the premature withdrawal of the drug will result in their reappearance. The average time period for healing was about eighty days. These results are interesting and important. The institution of streptomycin therapy is not undertaken lightly, for reasons which should be too well known to require reiteration, but with sufficient bacteriological indication and control it would seem thoroughly justifiable to impress it into the management of this difficult condition.

PROTEIN COMES INTO ITS OWN.

PROTEIN carries in its name a dignity and station which it has not always been accorded. Its etymological forebear is the Greek *πρωτεῖος* (first), and yet there was a time within this century when the first was in many eyes the last; earnest physiologists showed cause why protein intake should be cut to a sorry minimum, and equally earnest physicians found it the source of decomposition products which through "intestinal autointoxication" devastated the human economy. Today it is held in high and growing esteem among food elements, and this and every other medical journal publishes papers affirming and expounding its great importance in health and sickness. This dietetic progress is discussed in interesting detail by J. S. McLester[1] in a paper read before the Section of Internal Medicine at the Ninety-Seventh Annual Session of the American Medical Association in June, 1948. McLester finds five periods in the development of the science of nutrition. The first, the energy era, was the time of the great pioneer students of metabolism, who carried into the investigation of the living body the great chemical advances of their day which had begun with Lavoisier. A great deal of what is still the fundamental knowledge of metabolism came to light in that nineteenth century period. During this era, McLester points out, prime consideration was given to energy exchange, and attention to calories came first. However, despite all the discoveries of this period concerning the harmful effects of starvation, many doctors in the early part of the present century were still giving little thought to the nutritive requirements of the sick person. "They told the patient what he must not eat, not what he must eat." Two notable and disastrous examples of starvation diets were those allowed to patients with typhoid fever and with peptic ulcer. However, as the true position came gradually to be understood, more liberal diets were prescribed with benefit instead of with the harm that was feared. So came the second period, the period of adequacy of diet, when dietary measures came into the field of treatment of disease to challenge the overruling position held by drug therapy ever since the teachings of Hippocrates had fallen into neglect. The third era, the period of economy in nutrition, brought protein into disrepute. The apostles of "intestinal autointoxication" were teaching the evils of the absorption from the bowel of products of protein decomposition, and several quite eminent physiologists, as the result of personal and group experiments, concluded that restriction of protein in the diet (and it was severe restriction) promoted health and a sense of well-being. Although these views did not obtain general scientific acceptance, they had a considerable following amongst medical and lay people. The fallacies in the experimental conclusions were, apparently, the lack of controls and the shortness of the period of observation. It was eventually shown by animal experiment that substandard diets might not produce ill effects for long periods (5% of normal life expectancy according to one investigation), so that no reliance could be placed on observations made over a few months. Statements of the harmful effects of much protein in the diet on the kidneys and arteries have failed to stand up to theoretical analysis and have not been supported by careful and prolonged observations of persons receiving an exclusive meat diet. The theory of "intestinal autointoxication" was also completely discredited in scientific eyes, but along with the suspicion of danger from too much protein, it has lingered in popular thought. The fourth era, "the most colorful of all", was the vitamin era. This is too recent to need much comment. It included many discoveries of great and lasting importance and fired the public imagination; the result was in many ways unbalanced, but the position is now becoming stabilized. McLester sees two conservative tendencies in the present adjustment stage: first, the recognition that if a person is well nourished and his vitamin equipment adequate, then no nutritional benefit will accrue from the further taking of these substances, and, second, the recognition that man should, as a rule, take his vitamins in the form of natural foods. "The vitamin era is being rounded out with a wholesome appreciation of the importance of simple, good food."

It will be recognized that these four periods suggested by McLester are not mutually exclusive, nor are they all clearly delineated, but they may well be regarded as covering the influential lines of thought on nutrition and as reaching their peaks in a chronological order; they provide a progressive line of ideas leading up to the fifth and present period, the protein era. This has stolen on us in a quiet fashion. Protein, the old and familiar servant, has become respected and important, and we do not quite realize that it was not always that way. Beginning with the discovery of the indispensability of certain amino acids in 1938, understanding of the high value of protein has spread to many parts of medicine and surgery. The part played by protein in the metabolism of the cell has been greatly clarified in recent years, and the present concept is that the proteins of the body cell are not the fixed parts of a permanent structure, but are labile substances in a constant state of change; an adequate supply of these substances is essential to life. Protein has been shown to be of great value to both mother and child during pregnancy, and the old concept that protein predisposed to toxæmia of pregnancy appears to have changed to the directly opposite view. Accumulating evidence indicates that protein plays a fundamental role in the maintenance of both natural and acquired resistance to infection, being concerned, it would appear, in the efficiency of phagocytic activity and, more important still, in antibody formation. In the field of surgery proteins have come into great esteem, being, in the words of Co Tui, quoted by McLester, "essential to wound healing, to the maintenance of tissue integrity, and from present indications, to expeditious convalescence". Medical opinion has revised its restrictive attitude towards protein in the diet of nephritic patients; benefit appears to have followed increased protein intake by patients with peptic ulcer, so-called neurasthenia, pellagra and nutritional forms of œdema. Most dramatic, of course, has been the reversal of ideas in the liberal administration of protein to patients with liver disease; but the present attitude appears to have been amply justified by results. The present role of protein in health and disease was discussed in papers by F. S. Hansman and A. W. Morrow published in this journal on March 6, 1948, and the causes and treatment of protein deficiency were considered fully in a paper by James Isbister published in the issue of March 20, 1948. Our readers are referred to those papers and to the discussion which followed the reading of the papers of Hansman and Morrow at a meeting of the New South Wales Branch of the British Medical Association. The subject is one of great interest. No doubt there will be those who will extend the application of present-day concepts of the value of protein far beyond the justifiable limit and perhaps there will be a reaction. One cannot help feeling, however, that the place now won by protein after so many years of routine and even lowly service is more likely to be permanent than that of an untried though more spectacular *parvenu*.

[1] *The Journal of the American Medical Association*, April 2, 1949.

Abstracts from Medical Literature.

PÆDIATRICS.

Cirrhosis of the Liver.

P. D. KELLER AND W. L. NUTE, JUNIOR (*The Journal of Pediatrics*, May, 1949), discuss cirrhosis of the liver in children. Forty proved cases of cirrhosis from the records of the St. Louis Children's Hospital have been classified and discussed. Clinical and pathological findings have been outlined and brief comparison is made with the picture in adults. The authors state that cirrhosis in children is rare, but not so rare as has been supposed. Defined as a diffuse fibrosis of the liver, it can be brought about in a variety of ways, some of which depend upon inheritance and some upon major derangement in some other organ system. The classification used by the authors is ætiological in general; its limitations are those of the material at hand, which, although unusually large, is not representative of all known forms of the disease. Obstructive biliary cirrhosis is due almost always to congenital anatomical anomaly. Clinically it is distinguished by an obstructive type of jaundice in the newborn infant and pathologically by interlobular fibrosis, bile stasis and moderate inflammatory infiltration. Nodular cirrhosis usually develops in childhood rather than in infancy, and is insidious in onset. Jaundice and hepato-splenomegaly are the most constant findings. The atrophic stage is rare. The liver shows extensive perilobular fibrosis, focal regeneration and mononuclear cell infiltration without bile stasis. Cirrhosis is a rare sequela of *erythroblastosis fœtalis*. In addition to the usual clinical and pathological findings of erythroblastosis there is diffuse fibrosis of the liver. Congestive cirrhosis is the result of repeated severe passive congestion of the liver that alternates with periods of relative compensation. Clinically it is overshadowed by the primary disease of the heart. The excess fibrous tissue is central to the lobule rather than diffuse or peripheral. Hyperæmia and dilatation of the sinusoids are typical. The liver is enlarged rather than shrunken. Hepatic vein thrombosis as a cause of congestive cirrhosis is rare. A variety of toxins are capable of causing necrosis in the liver, which, if it is not too excessive, is followed by fibrotic repair. There seems to be nothing distinctive about this sequence as it occurs in children. Two typical cases of hepatolenticular degeneration are described. So far as the liver is concerned they are indistinguishable from ordinary nodular cirrhosis. The incompleteness of our understanding of this field is emphasized by the presentation of seven unclassified cases, which illustrate the difficulties in exact diagnosis.

Ovarian Tumours in Infants and in Children.

M. E. COSTIN, JUNIOR, AND R. L. J. KENNEDY (*The American Journal of Diseases of Children*, August, 1948) discuss the incidence of ovarian tumours in infants and children. Besides reviewing the literature on the subject, they have reported data on 22 cases of ovarian tumour occurring in infants and children fourteen years of age and younger in which treatment was carried out at the Mayo Clinic during the past twenty-eight years. More than 200 cases of ovarian tumour in infants and children have been reported in the literature. In approximately one-third of these the tumours were simple multilocular cysts, in one-fourth dermoid cysts, in more than one-third carcinoma or sarcoma. In recent years the diagnosis of sarcoma and carcinoma of the ovary in children has become much less frequent, and it seems likely that many of the tumours which were reported as sarcoma or carcinoma in the older literature were granulosa-cell tumours or dysgerminomata. The authors state that simple cysts are relatively common ovarian tumours in infants and children. In their series of 22 cases seven were of simple cysts. Pain in the abdomen is the outstanding symptom, and torsion of the pedicle is a frequent complication. The latter event occurred in five of their seven cases. Simple cysts with twisted pedicles are frequently confused clinically with appendicitis or appendiceal abscess. Cystadenoma of the ovary is rare in children. The three in this series were all in children fourteen years of age who had reached the time of puberty. Cystadenocarcinoma of the ovary in children is correspondingly rare. Teratoma is the commonest ovarian tumour in children. In the series there were 10 cases. The dermoid cyst variety of teratoma was commoner than the embryonic type; there were seven cases of dermoid cysts and three of embryonic teratoma in the series. The predominant symptoms are abdominal tumour and pain. Radiograms are useful adjuncts to the preoperative diagnosis of dermoid cyst. The dermoid cyst type of teratoma is usually benign, but the embryonic type must be considered as potentially malignant and frequently is. One case of dysgerminoma occurred. It is pointed out that dysgerminomata are unusual in that they frequently are associated with pseudohermaphroditism or genital hypoplasia. Opinions concerning the malignancy of dysgerminomata vary, but it is safest to consider them as definitely malignant tumours and to treat them as such with radical surgical procedures and post-operative X-ray therapy. Granulosa-cell tumours may occur in infants and children of any age, but are uncommon. There was one case in this group. Granulosa-cell tumour is a rare cause of sexual precocity in children and must be considered in the differential diagnosis of this condition. The incidence of malignant granulosa-cell tumour in children is low.

Antihistaminic Drugs.

L. H. CRIEP AND T. AARON (*The Journal of Pediatrics*, April, 1949) discuss the use of the antihistaminic drugs in the treatment of allergic diseases of childhood. In particular they discuss a new drug, "Neohetramine", available as an elixir and as tablets. The therapeutic results they obtained with this drug in providing symptomatic relief, particularly of hay fever, allergic rhinitis and urticaria, were at least as good as those obtained with other antihistaminic drugs. They state that it possesses real advantages, however, in that it produces less unpleasant side reactions and so is safer and easier to use. Careful observation of children receiving the drug over periods as long as three months failed to reveal any effect on blood pressure, pulse rate, urine or blood count. The dose given was one drachm of the elixir (25 milligrammes) every four hours for infants up to four years of age and 50 milligrammes each four hours to older children. When relief was obtained it lasted, as with the other antihistaminic drugs, for a period of three to six hours.

SAMUEL J. LEVIN AND SELMA S. MOSS (*The Journal of Pediatrics*, May, 1949) report similar satisfactory results with another new drug, "Thephorin". It was found very effective in hay fever, asthma, allergic rhinitis, infantile eczema and urticaria. It produced side reactions, drowsiness, abdominal pain, constipation or excitement in 20%, but needed to be discontinued in only 8%.

Jaundice in the Newborn.

GLADYS J. FASHENA (*The American Journal of Diseases of Children*, August, 1948) states that it has been suggested that the hyperbilirubinæmia that is found almost constantly in newborn infants is due to hæmolysis, and this is probably partly so, for there is a steady fall in red cell count during this period. However, no close relationship between the fall in the number of red cells and the degree of jaundice has been demonstrated. An alternative explanation depends on immaturity of the liver, resulting in impaired excretion of bile pigment, but liver function tests have failed to demonstrate deficient liver function. Recently it has been suggested that all neonatal jaundice, physiological as well as pathological, is hæmolytic in origin and is due to incompatibility between fœtal and maternal blood. The author has reinvestigated the problem. She failed to find any accurate correlation between the degree of jaundice and the fall in red cell count, nor was there any greater incidence of jaundice in a group of babies whose A, B or Rh blood group differed from that of their mothers. However, direct assessment of hepatic function from determination of the velocity constant of excretion of bilirubin showed impairment of liver activity in babies with pronounced hyperbilirubinæmia and normal excretory function in a comparable group without hyperbilirubinæmia. This result indicates that liver immaturity is at least one factor in the production of physiological jaundice of the newborn.

ORTHOPÆDIC SURGERY.

The Accessory Tarsal Scaphoid.

I. ZADEK AND A. M. GOLD (*The Journal of Bone and Joint Surgery*, October, 1948) discuss the exact relation of the accessory scaphoid to the scaphoid bone and to the *tibialis posterior* tendon. Microscopic studies showed that the accessory scaphoid and the scaphoid bone, having the usual cancellous trabecular structure of tarsal bones, were joined by a layer of soft tissue, which consisted of hyaline cartilage, dense fibrocartilage, or a mixture of the two. In none of the cases studied was a well-developed, freely movable joint found, with smooth hyaline articular cartilage capping each bone, and with the two articulating bones bound together by a synovia-lined fibrous capsule, such as one would expect to find in the talo-navicular joint. The

authors state that in some cases, at the time when growth ceases and the epiphyses of the skeleton close, or soon thereafter, ossification of the intervening plate between the accessory scaphoid and the scaphoid bone stops without the plate's having been completely ossified, so that a synchondrosis remains. In most of these cases, in which there is an accessory scaphoid, the *tibialis posterior* tendon is attached to the scaphoid tubercle to a greater degree than normally exists.

Tenosynovitis of the Extensor Carpi Ulnaris Tendon Sheath.

D. D. DICKSON AND C. A. LUCKEY (*The Journal of Bone and Joint Surgery*, October, 1948) describe the clinical picture produced by tenosynovitis of the *extensor carpi ulnaris* tendon. The patient usually has a twisting injury of the wrist, followed at a varying interval of time by pain, deep in the wrist joint and aggravated by all wrist motions. Later, swelling may be noted about the distal end of the ulna. Night pain may or may not be noted. Subjective sensory disturbances along the distribution of the dorsal cutaneous branch of the ulnar nerve may be present; they are described by the patient as "numbness" and "tingling". Examination reveals tenderness along the course of the *extensor carpi ulnaris* tendon and swelling about the distal end of the ulna, as well as grating within the sheath on motion of the tendon. Repeated observations may be necessary to ascertain this fact. Flexion and extension of the wrist, especially against resistance, as well as ulnar and radial deviation of the wrist against resistance, usually produce the pain, as may also pronation and supination. Localization of the pain, by the patient, deep in the wrist, should make the examiner check carefully for this condition. Œdema of the surrounding subcutaneous tissue has been present in all the authors' cases. The dorsal branch of the ulnar nerve is situated in the œdematous tissue and this may account for the ulnar nerve symptoms of which the patient complains. The authors consider that hæmorrhage, which probably takes place in the sheath at the time of injury, produces a non-specific inflammatory reaction in the synovial tissue. The long and very confined fibrous sheath through which the tendon glides is a most important factor in producing the tenosynovitis and also in keeping the condition active. The authors believe that the condition is often overlooked and that involvement of the triangular ligament of the wrist joint is often diagnosed in error. Residual pain following Colles's fracture, in some instances at least, is due to a tenosynovitis of the *extensor carpi ulnaris* tendon. The treatment is operative removal of thickened synovial tissue after the fibrous tunnel has been incised throughout its entire length. Dislocation of the tendon is prevented by suture of dorsal carpal ligament over the split sheath.

Arthritis Deformans of the Hip Joint.

P. E. LUGIATO (*The Journal of Bone and Joint Surgery*, October, 1948) states that the essential alterations in *arthritis deformans* of the hip joint are traumatic in origin and include degenerative and proliferative changes, erosion of the cartilaginous and superficial bony strata, and loss of elasticity of the joint components. The fibrillar system constitutes the supporting framework of cartilage, the early weakening of which indicates loss of cartilaginous elasticity. Loss of elasticity is followed by erosion, marginal proliferation and, in the later stages, invasion and replacement of cartilage by connective tissue. The degenerative process begins with the alteration of the fibrillar system of support. Degeneration increases with further alterations in the fibrillar system and ends with the destruction of the joint surface. In studies of the fibrillar system in articular cartilage by the polarized-light method it was demonstrated that changes in arrangement of the collagenous fibrils appear very early in the evolution of *arthritis deformans* and constitute the first signs of degeneration. The author points out that when the ordinary methods of staining are employed fibrils are apparent microscopically only in the very late stages of degeneration, when there has been extensive destruction of the cartilage layer.

Criteria for Spine Fusion after Removal of Protruded Nucleus Pulposus.

G. A. CALDWELL AND W. B. SHEPPARD (*The Journal of Bone and Joint Surgery*, October, 1948) review 75 cases of protrusion of a *nucleus pulposus* proven by operation. In all cases laminectomy with spinal fusion had been performed three to seven years previously. They conclude that excellent and satisfactory results can be obtained in as high a percentage of cases by laminectomy alone as by the combined operation. Hypertrophic changes of variable degree, with or without narrowing of the disk, occurred in over two-thirds of the cases studied. Functional end results do not correlate with or depend upon the presence or extent of such post-operative changes. The end results are not significantly related to the existence of anomalies. Recurrences took place in 8% of the cases studied, but did not seem to be related to the presence of anomalies or post-operative narrowing of the disk and hypertrophic changes. Results were excellent in 42% of cases, satisfactory in 40%, unsatisfactory in 17%. Spinal fusion was performed only if disabling backache persisted for a year or more after laminectomy. The authors believe that most of the unsatisfactory results (other than recurrence of protruded disk) were such that spine fusion would not have improved them.

Supracondylar Fractures of the Humerus Treated by Kirschner-Wire Transfixion.

A. L. SWENSON (*The Journal of Bone and Joint Surgery*, October, 1948) states that the use of transfixing wires in the treatment of difficult supracondylar fractures of the humerus in children is especially useful for patients who have such extensive swelling about the elbow, when first examined, that immobilization in acute flexion, after closed reduction, cannot be carried out. Olecranon-wire traction is not necessary, since the transfixing wires maintain the original reduction until union occurs. The danger of Volkmann's ischæmia is lessened, since splinting in acute flexion is not necessary. Ten patients, first examined from two to six days after injury, have been successfully treated by this method of blind pinning. The author states that, after the fracture has been completely reduced, the insertion of the transfixing wires is not difficult. The reduction is checked by radiography, and if this is satisfactory one short Kirschner wire is drilled through each condyle, across the fracture line, and into the humeral shaft. The technique is described in detail. Because of the forward curve of the distal end of the humerus and the increased width at the condyles, the wires must be directed slightly posteriorly and inward, at an angle of 30° or 40° with the humerus, so that the shaft will not be missed. Properly placed, they penetrate the medial and lateral condyles where the common flexor and the common extensor tendons attach themselves; they do not enter the elbow joint. They should be inserted in the bone just beneath the condylar ridges and should strike the opposite side of the humerus about one and a half inches above the fracture line. When they are in satisfactory position (confirmed radiographically) they are cut off at the skin surfaces and skin is pulled over them. A posterior splint is then applied with the elbow in 90° flexion. The wires are removed in about three weeks under local anæsthesia; the splint may be retained for a few days longer. The author states that no cases of injury to the ulnar nerve were encountered, and after removal of the splints the patients made satisfactory progress in regaining elbow motion.

Intracapsular Fractures of the Femur.

J. PATRICK (*The Journal of Bone and Joint Surgery*, January, 1949) states that he has treated all intracapsular fractures of the neck of the femur with a Smith-Petersen nail and a fibular graft since 1942. There were 107 cases, but death due to operation (mortality 8%) and to natural causes reduced the number of two-year follow-up cases to 47. Non-union occurred in 13% of cases. The author believes that the cases of non-union were accounted for by accident or errors of technique. Aseptic necrosis developed in 9% of cases and osteoarthritis occurred in 21%. In only two cases did the arthritis prove more than a minor disability. The author attributes the osteoarthritis to penetration of the joint by the graft. In the cases affected the graft was inserted rather close to the joint. To avoid penetration of the joint by the fibular graft it should be inserted to a depth of about a quarter of an inch less than the nail. Weight-bearing should be avoided for the first three months.

Residual Paralysis after Brachial Plexus Injuries.

A. M. HENDRY (*The Journal of Bone and Joint Surgery*, February, 1949) states that after brachial plexus injuries and other forms of paralysis of the upper limb, even when residual paralysis is very grave indeed, and even when the limb is almost flail, a forearm which can project forwards by the construction of a bone-block behind the elbow, with arthrodesis of the shoulder when necessary, a hand with fingers in the form of a claw and a thumb which opposes them, and a wrist which may perhaps be arthrodesed, but which still better can flex or extend when the forearm is pronated or supinated—these, together with the wise use of such muscles as are likely to gain function, may enable a patient to do very much more than he can with an artificial limb.

Special Article.

THE DIAGNOSIS OF POLIOMYELITIS.

IT has been suggested that, as the number of cases of poliomyelitis is once again assuming epidemic proportions, some reiteration of the various points which helped in diagnosis in other days may be appropriate.

To this end therefore this article has been prepared. It will be brief; it will be as dogmatic as possible, for a legion of "ifs", "buts" and "maybes" confuse and distract the mind; it will conclude with some observations upon the subject not intimately related to diagnosis.

It would appear that the most helpful method of approach would be to discuss each symptom and sign in sequence and to indicate the potentialities and fallacies of each as a diagnostic weapon.

Much of what follows emanates from observations published in greater detail in THE MEDICAL JOURNAL OF AUSTRALIA of August 20, 1938, page 276.

Clinical Types of Poliomyelitis.

It is wise to recall three groups in which the disease presents itself, in order that perspective shall be maintained:

Group I, consisting of cases of the mild undiagnosable, possibly afebrile illness sustained by many members of the community and conferring immunity.

Group II, consisting of cases of a febrile illness of rather greater severity than that of Group I, with some headache and slight neck stiffness and tending to complete recovery except in an occasional case in which very mild weakness appears and is manifest later. There were some unforgettable examples of this type in the 1937 epidemic, such as the following case. The suspect case having been found in a house of many children and it being decided that the patient was severely affected with gross paralysis, a query was made concerning the recent health of the other eight offspring. "Oh, they're all right, though little Willie hasn't been too good over the last week", was the mother's reply. Now little Willie, who was energetically contributing to the pandemonium in that sad little house, had a neck very nearly as stiff as his elder sister gravely stricken with the disease. Further, Willie developed no paresis, and his illness would have passed unrecognized if his sister had not developed her more severe condition.

Group III, consisting of the typical acute cases with a definite febrile phase followed by a paralytic phase. The febrile phase may be short (three to five days), it may persist irregularly for a maximum of thirteen days (the "straggling" type), or it may appear in two "humps", each lasting about three to five days, the second hump being more decided than the first and separated from it by two to three days of apparent normality. This is the "dromedary" type of Draper.

Incubation Period.

The incubation period has usually been regarded as approximately seven to ten days. In a recent Saint Helena epidemic there appeared evidence that one patient developed the disease four days after exposure, three others eleven, twelve and eighteen days respectively, and one apparently as late as thirty-one days.

The Symptoms.

Fever.

Fever is uniformly present at some stage in cases severe enough to produce symptoms. Its duration is three to thirteen days, sometimes with recession to normal for two to three days, as in the "dromedary" types. It is rarely above 103° F., and is usually 100° to 101° F. A temperature of 105° F. is unlikely to be due to poliomyelitis.

Rapid Pulse.

The pulse is rapid in proportion to the temperature, the average rate being 110 to 150 beats per minute.

Drowsiness.

Drowsiness is extremely common, but is coupled with great lucidity when the patient is roused. Orientation is excellent even with severe involvement. Bilateral facial weakness, pharyngeal and laryngeal involvement, inhalation of foodstuffs with subsequent pneumonitis and toxæmia therefrom may combine to produce a picture of semicoma, which is not one of the features of the disease.

Headache.

Headache is very common. It is usually frontal or supraorbital, occasionally vertical, and often intermittent.

Pain in the Back of the Neck and in the Back.

Pain in the back of the neck and in the back is probably the most important symptom if volunteered. It is present in a high percentage of "clinical" cases and even in the "accidentally" discovered cases occurring in the same house as the definite cases. It is not an agonizing pain; it is not sharp and lancinating; it is a dull ache aggravated by attempts at flexion of neck or spine. It is not accompanied by great local tenderness in the muscles. It is much more a symptom of poliomyelitis than of meningitis.

Muscle Pain.

Muscle pain, causing pains in the limbs *et cetera*, has always been regarded as a feature of the disease and is so to a degree. It does not appear to be of great severity and is not associated with severe tenderness. Later in the disease, in the absence of appropriate treatment, muscles may become excessively stiff and painful.

Abdominal pain sometimes is mentioned; it is probably a referred pain; it is occasionally induced when neck stiffness is being elicited.

Tremor.

Tremor is often a notable feature. It is of "intention" type and is seen in purposive movements; patients are liable to drop a glass of water *et cetera*. Tremor may be intermittent and vary in intensity from time to time.

Disturbance of Micturition and Defæcation.

With micturition there may be either some difficulty in commencing the act or failure to empty the bladder completely. A full painless bladder is commonly found.

Constipation is common; diarrhœa is excessively rare, and usually indicates another diagnosis.

Eye Symptoms.

Photophobia, squint and diplopia form rather a rare group in the early stages. Diplopia is not a symptom likely to be mentioned by children.

Paralytic Symptoms.

Paralytic symptoms are of vast importance in diagnosis. Typical expressions used by the parent are "He couldn't sit up this morning", "His leg seems floppy", or "He seems to be dragging his feet".

The "vocal" symptoms are important to recognize. There are two types: (i) the nasal voice of palatal involvement, such a voice following immediately upon a febrile upset being strongly suggestive of poliomyelitis; (ii) the croaky, husky weak voice of laryngeal involvement with a bovine cough usually associated. The presence of either of these "voices" imperatively demands strict observation, for if deglutition also is affected, as it often is, food given orally may pass into the respiratory tract with dire effect. The recognition of these "vocal" phenomena is of supreme importance; failure to recognize them may result in tragedy.

Squint and diplopia are comparatively rare. It is possible that diplopia occurs more commonly than is realized, as it is not a symptom mentioned freely by children.

Evidence of paralysis may appear as early as twelve to twenty-four hours from the onset of the febrile phase. This is unusual. A more usual time is from three to ten days after the onset of symptoms. Very mild palsies may not be recognizable for some weeks, when the stresses of active life indicate past damage.

Paralysis tends to be maximal within a short period from its onset. Slowly progressive weakness developing over many days is not due to poliomyelitis.

Marked symmetry or a hemiplegic distribution of the weakness is not characteristic of poliomyelitis.

Points in the Examination.

There is great variation in the presenting features in early poliomyelitis, but the following is a reasonably accurate summary in the average case.

1. The child is flushed, sweating and ill, though well orientated and cooperative (except the child in the under three years age group). The temperature is 100° to 103·5° F., rarely higher. The pulse is rapid in rate (120 to 150 per minute). There is no cough or coryza, except with coincidental infection or as a result of causes indicated above.

2. The throat may be engorged, but exudate on the tonsils suggests another diagnosis.

3. The heart and lungs are clinically normal (unless there has been inhalation of foodstuffs). There may be unilateral or bilateral impairment of chest movement if there is intercostal involvement.

4. Examination of the abdomen may show a full, painless bladder, but no other abnormality. A palpable spleen is against the diagnosis.

5. The extremities are the most readily assessable regions in which to detect paresis. In the early stages no involvement will be detectable. Rarely, paralysis will appear within twenty-four hours of the onset of fever.

6. Reflexes are of great importance; asymmetrical diminution or absence may be decisive in the diagnosis. Inability to extend the knee joint, if due to poliomyelitis, will be accompanied by absence of the knee jerk; if it is due to myalgia, fibrositis or hysteria, the reflex will be hyperactive.

The Signs of Central Nervous System Irritation.

The Spinal Signs.

The spinal signs are of great diagnostic importance in the preparalytic phase. In their complete absence it is almost impossible to make a positive diagnosis.

Neck Stiffness.—Inability to approximate the chin to the *manubrium sterni*, or the nose to the knee whilst sitting with the knees drawn up, constitutes neck stiffness. If these tests are readily performed there is no neck or spine stiffness present. In apparent neck stiffness there must be a free lateral roll of the head about the long axis of the body; restriction in this movement suggests a local lesion, such as fibrositis. There may be great difficulty in the uncooperative age group in assessment of the result, but this may be overcome by placing a lighted torch in the region of the navel and watching the movement of the head as the sitting child looks down. This is a purely objective test of great value.

Head Retraction.—Head retraction is not present.

Localized Tenderness.—Localized tenderness of the neck and spine muscles is not present.

Kernig's Sign.—Kernig's sign is not particularly helpful, owing to individual variation in ability to extend the knee with the thigh flexed at the hip. When it is present, the other "spinal" signs are always present and more definite.

The Cerebro-Spinal Fluid.

Characteristically there is an increase of cells in the cerebro-spinal fluid up to a maximum of 2000 per cubic millimetre. Lymphocytes and mononuclear cells predominate, though in some cases in the pre-paralytic stage polymorphonuclear cells may make up 50% of the count. It has been observed that the polymorphonuclear cell count tends to fall rapidly after withdrawal of the fluid; it should therefore be examined as soon as possible after lumbar puncture. After paralysis appears the count falls and the polymorphonuclear cells disappear.

The protein content of the cerebro-spinal fluid approximates to normal in the pre-paralytic stage, but tends to rise in the paralytic phase; it often continues to rise coincidently with the falling cell count. Greenfield and Carmichael noted amounts up to 300 milligrammes *per centum* eight weeks after the onset of the disease. The protein content finally returns to normal.

Chloride and sugar levels are normal throughout.

As a means of diagnosis in the period under discussion, that is, the early pre-paralytic stage, examination of the cerebro-spinal fluid has considerable use if combined with the history and clinical examination, and does serve often to differentiate the case of purulent meningitis in the difficult period under three years of age, and helps in the cases of meningismus.

But there are fallacies, the following being examples. (i) Single examinations of the cerebro-spinal fluid may well show a normal cytological state in the early stages, but such a finding does not exclude poliomyelitis. One observer states that in 10% of cases normal fluid is found throughout; this, however, is difficult to assess unless many examinations are made. (ii) Other conditions may produce fluid of similar type, for example, early tuberculous meningitis, benign lymphocytic meningitis and cerebral abscess in its "walled off" stage. (iii) A "bloody tap" can be a similar sort of nuisance.

Negative Signs.

The following signs, if present, tend to negate the diagnosis:

1. Cough, unless with a coincident respiratory tract infection or as the bovine cough of laryngeal involvement, in which case the diagnosis is usually obvious.

2. Diarrhœa, unless produced by purgation.

3. Mental clouding. This is very rare. Mild delirium at night occasionally occurs, but usually the mind is extraordinarily clear.

4. Convulsions. These always suggest another diagnosis.

5. A rigor.

6. A rash. This is not seen except with coincident impetigo, scabies, hives *et cetera*.

7. A palpable spleen. This indicates another diagnosis.

8. A limb described as "stiff". This suggests trauma or a local inflammatory lesion. An affected limb in a case of poliomyelitis is always described as "weak", "floppy" or "flabby".

9. Known persistence of fever after twelve days. The temperature is usually normal by the fifth to the eighth day. Rarely pyrexia lasts to the twelfth or thirteenth day. A complication, such as the inhalation of food *et cetera*, would modify this rule.

Points of Interest not Particularly Related to Diagnosis.

Spread of Infection.

The two probable methods of spread of infection are by droplet infection from the nose and throat, and by contamination from infected fæces, via fingers, food or flies, as in typhoid.

Virus can be isolated from the naso-pharynx of patients five days prior to the onset of symptoms and five days after; from the fæces for from three to twelve weeks after the onset of symptoms. It can regularly be isolated from the fæces of intimate family contacts (who may or may not be symptomless) for as long as eight weeks after the onset of symptoms in the original case. Rarely it can be isolated from the throats of such contacts.

The infectivity in a given case corresponds fairly accurately with the periods during which virus can be isolated from the naso-pharynx, that is, five days before to five days after.

Virus has been isolated from the sewage of cities and towns during epidemic periods, but not otherwise. There are very few authentic examples of milk-borne disease, and no proof of water-borne infection. After the feeding of infected human stools to the blowfly, virus could be detected in the excreta of the fly for three weeks. The fly therefore may play some part in the spread.

Prevention of Spread.

It is a striking point that all measures enforced to endeavour to prevent the spread of poliomyelitis have had uncertain success, though it is not surprising when so many cases can be subclinical in type.

Effective isolation of contacts of an infected patient would involve the whole family for a period up to eight weeks; this is, of course, impracticable. The closing of schools does not keep children apart. The closing of fresh-water swimming baths would seem a rational measure.

In the specific instance of how to instruct the family contacts in a definite case when the patient has been removed to an isolation hospital, it is reasonable to suggest that other children remain isolated at home for two weeks, at the end of which time either they will have had the disease or, if they have not developed it, the naso-pharynx should be clear of infection. The parents will of necessity continue their manifold duties. It is not practical to suggest otherwise. The fact that any member of the family may carry virus in the fæces for some weeks should not prove dangerous with modern sanitation and hygiene.

Pathogenesis.

From immunity surveys it is estimated that for every clinically recognizable case there are 1000 subclinical examples of the disease.

Violent exercise during the early phases of the disease appears definitely to predispose to increased severity of paralysis. Hence the suggestion that violent competitive sport be curtailed in schools during epidemic periods, though there must be many difficulties associated with such an edict.

The route of infection of the central nervous system is thought to be via the axons of the nerves supplying the throat, not via the olfactory bulb.

Immunity.

After an attack, immunity is of long duration, probably for life. Second attacks, though excessively rare, have occurred.

Prophylactic vaccines have been produced which have been effective in monkeys; a human trial has not yet been attempted.

Tonsillectomy and Poliomyelitis.

There seems little doubt that if, by ill luck, virus should be present in the naso-pharynx at the time of tonsillectomy operation, or should appear there shortly thereafter, severe bulbar poliomyelitis is likely to follow. Some risk probably also applies to breaches on the oro-nasal mucous membrane from operations or dental extractions.

Johnston's Utah figures (1943) are most instructive in this regard. He records that the poliomyelitis-tonsillectomy ratio before an epidemic of poliomyelitis occurred was 0·7:1000; the ratio during the epidemic was 25·5:1000, and 43% of all cases of bulbar involvement in that epidemic followed tonsillectomy. The incidence of poliomyelitis was 2·6 times, and the incidence of bulbar involvement 16 times greater in the children who had recently undergone tonsillectomy than in the general child population.

The Cunning Survey of 1947, which purports to show that the risk of tonsillectomy is exaggerated, is based on inadequate statistical control and is regarded in many quarters as dangerously misleading.

There are, of course, cases in which the adeno-tonsillar pathological state is so gross and so likely to provide serious complications that tonsillectomy is justifiably regarded as a matter of some urgency. Any decision to operate in such cases during epidemics of poliomyelitis must be made with due regard to the figures stated above, and with full cognizance of the fact that there is a definite risk involved. Discussion of the risk with parents would appear to be indicated.

Melbourne. MOSTYN L. POWELL

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on Saturday, June 25, 1949, at the Wimmera Base Hospital, Horsham, the President, DR. DOUGLAS THOMAS, in the chair. In the afternoon, members of the medical staff of the hospital presented a series of clinical demonstrations and in the evening DR. CLIVE FITTS discussed a number of recent cardio-respiratory developments and delimited the value and usefulness of some of the aids used in the investigation and diagnosis of certain chest complaints.

Intermittent Crippling Pain in the Legs.

DR. B. HUTTON JONES showed a male patient, aged fifty-four years, proprietor of a sports store, who was the subject of severe intermittent pain in the legs. He had been athletic when younger and was reasonably well until he was forty-eight years of age, though he admitted undue weariness then, after a day's quail-shooting. Soon afterwards, when he was oiling cricket bats one day, he felt a sickening pain deep-seated in the chest and upper part of the abdomen; it was necessary for him to stop his work and rest, and he became cold and clammy, but the pain did not radiate past his shoulders or affect his arms or legs. He gave up golf and shooting, restricted his efforts and took trinitrin occasionally for substernal pain. Early in 1947 he consulted a medical specialist in Melbourne and the diagnosis of *angina pectoris* was established, supported by electrocardiographic findings. He went on to Portland for a holiday, became ill, consulted Dr. H. B. D. Vaughan and was kept in bed for six weeks. He restricted his efforts further and was not seriously upset until early in 1948, when he first noticed that he could not walk fast without contracting severe pain in each leg. The pain was cramp-like and he had to stop walking immediately. He did not have any pain when at rest or in bed at night. He did not notice any abnormal appearances in the limbs. Dr. Hutton Jones said that the patient had read with interest the published accounts of the recent illness of King George VI and had consulted several doctors to see if an operation was likely to help him. While in Melbourne for that purpose, he had contracted pneumonia and pleurisy and was confined to bed for some time. Three weeks before the meeting, he had returned to his home at Horsham and, within a week, for several nights he had excruciating pain, commencing in the toes of the right foot, spreading to the sole and around the instep and up the leg to just below the knee. He could get relief only by rising from bed and walking about. His general health was better than it had been for two years. His appetite was good and the actions of bowel and bladder were normal. When first examined by Dr. Hutton Jones the patient was a well-built man, but did not look well; though not anæmic, his complexion was greyish. The apex beat was in the sixth intercostal space, approximately four and a half inches from the mid-sternal line; some extension of cardiac dulness to the right was detected, but no bruits were audible. Irregularly recurring extrasystoles were felt at the wrist, and there was some thickening of the arterial walls. The blood pressure, measured in the right arm, was 120 millimetres of mercury (systolic) and 85 millimetres (diastolic). Measured in the left arm, the readings were 110 and 75 millimetres of mercury respectively. On examination of the *fundi oculorum*, some vitreous opacity was seen with faint "silver wire" arterial changes and fullness of the veins, but not any retinitis or changes in the optic disks. Relative dulness and some diminution of breath sounds were noted in the lower lobe of the right lung, which was the site of the recent pneumonia. Neither liver nor spleen was demonstrably enlarged and nothing of an unusual nature was found on examination of the abdomen or of the urine. The lower limbs were of good colour, but were about two degrees cooler than the axillæ. The popliteal, posterior tibial and *dorsalis pedis* arteries were not palpably thickened. The tendon jerks at the knees and ankles were elicited readily; no sensory changes were found. Blood specimens failed to yield the Wassermann or Kahn reaction. Hypertrophy of the left ventricle was demonstrated from the skiagrams. Electrocardiographic tracings showed left axis deviation with slurring of the *QRS* complex, an inverted *T* wave in Lead I, a diphasic *T* wave in Lead II, a prominent *P* wave in Leads I and II, and frequent ventricular extrasystoles. Dr. Hutton Jones emphasized the severity of the angina, with severe crippling pain, if the patient walked forty paces, and the relief obtained from the pain in the legs by walking about. He suggested that the man had originally had hypertension and a coronary occlusion, and invited information and advice as to what should be done for him.

DR. C. H. FITTS said that he was diffident to make a diagnosis or to offer advice. When in England recently he had gathered that the King's illness was of longer duration than had been announced officially, that numbness had preceded the pain, and that the present was a vascular problem. At the Royal Melbourne Hospital he had come across crippling intermittent claudication without vascular lesions and he thought that the administration of quinine hydrochloride in five-grain dosage had helped. He doubted whether the operation of sympathectomy was indicated for the patient under consideration. He believed that, at some time, the patient had had an anterior infarction.

DR. ROBERT SOUTHBY referred to the relief of nocturnal cramp by means of the administration of five grains of calcium gluconate three or four times daily.

DR. DOUGLAS THOMAS remarked that coronary disease *per se* did not produce any change in the size of the heart. From a study of the skiagrams shown he thought that the patient had thickening of the wall of the left ventricle and presumably had had a high blood pressure at some time. Recent work on the slurring of the *QRS* complex had shown an intensity of the flow of stimuli; there was a gross variation in the rate direction of the wave corresponding to slurring. With reference to the lower limbs, Dr. Thomas expressed the opinion that there was some degree of arteriosclerosis present; he commented that relief of the pain by walking was not uncommon, as activity stimulated an improvement in the minimal flow of blood, the marginal effort relieving the pain; if the patient continued the walking the effort would produce intense pain again.

Puerperal Pyo-Pneumothorax.

DR. THOMAS WALPOLE showed a married woman, aged twenty-two years, who, within twenty-four hours of delivery, had suddenly developed acute pain in the left side of the chest with blood-stained sputum and signs of consolidation towards the base of the lung. She had been admitted to the Wimmera Base Hospital on February 17, 1949, the membranes having ruptured ten days previously, and was delivered next day of a seven-month premature baby, who lived only for several hours. On February 25, from skiagrams, the presence of the consolidation was confirmed, together with a small amount of air in the pleural cavity and collapse of the upper lobe of the left lung, with shift of the mediastinum to the right. The temperature was elevated, but subsided after penicillin was given from February 22 to March 7. On March 1 an unsuccessful attempt was made to aspirate the chest. Dr. Walpole said that the temperature had risen again and, from skiagrams prepared on March 15, it was adduced that the left lung had collapsed to a great extent, that the left capola of the diaphragm was raised because of adhesions to it, and that the mediastinum was in the mid-line of the body; a fluid level could be seen.

From March 15 till April 1 a course of sulphamerazine and sulphadiazine was given without improvement, and on March 23 aspiration was again attempted fruitlessly. From a skiagram prepared on March 28 it was apparent that the fluid had reached the level of the sixth rib posteriorly. Twelve ounces of thin purulent fluid were removed by aspiration on April 3; attempted culture for tubercle bacilli failed, but staphylococci and pneumococci were identified. Fifty thousand units of penicillin were injected into the cavity after aspiration on April 3; subsequently the fluid level fell to the seventh intercostal space, but soon rose again. Aspiration was performed again on April 13 and one ounce of blood-stained fluid was obtained with similar bacteriological contents. The temperature range was lower, under the influence of penicillin, from April 2 to April 13, but rose again. From skiagrams prepared on April 21 it was adduced that the left lung was almost completely collapsed by pneumothorax and that very little fluid was present in the pleural space. A third course of penicillin was given from April 21 to May 1, and the temperature became normal and did not rise again prior to the discharge of the patient from hospital on May 16; by then the lung had reexpanded satisfactorily. Dr. Walpole added that he had examined the patient again on June 20 when she was afebrile and well; the lung was reexpanding nicely, but a faint fluid level was detectable in the skiagrams. During the course of the illness it was established that the serum failed to yield the Wassermann reaction; on two occasions a fruitless search for tubercle bacilli had been made in preparations of specimens of sputum; the Mantoux reaction was not obtained with dilutions of one in a thousand or one in a hundred parts. The dosage of penicillin used was approximately 20,000 units every four hours in each of the three courses of treatment. Dr. Walpole invited comment on the possible presence of a tuberculous element in the condition, reasons for the occurrence of the pyo-pneumothorax and advice on the future management, especially if the fluid formed again.

DR. DOUGLAS THOMAS postulated the occurrence of a venous embolism as the underlying complication and discounted the likelihood of any tuberculous factor. He thought that the sequence of events was thrombosis in the pelvic area, embolus to the lung with pneumonitis and infection of the pleural cavity.

DR. ROY WATSON said that he was in general agreement with what Dr. Thomas had said, but it seemed likely that the infection of the lung was metastatic with abscess formation and connexion with the pleural cavity; the association of abscesses of the lung and brain was well known and was attributed to multiple metastasis.

DR. CLIVE FITTS said that it could be demonstrated from the skiagrams that the original shadow was intrapulmonary and the later ones were extrapulmonary. He commented that the case had been well handled; the patient was afebrile and felt well, and all that was still necessary was continued observation with further fluoroscopy and skiagrams.

DR. ROBERT SOUTHBY said that pulmonary embolism was a definitely recognized complication of pregnancy especially when manipulative interference occurred. The patient might have inhaled vomitus, which could have led to infection of the lung; that process was also worthy of consideration. He thought that Dr. Walpole should be on the watch for localization of a collection of purulent material and, if it was deemed necessary, he should be prepared to use penicillin again in adequate dosage.

In reply, Dr. Walpole thanked those who had contributed to the discussion and stated that the facts of the case were against the inhalation theory.

Paget's Disease of Bone.

Dr. Walpole also showed a male patient, aged fifty years, whom he had first interviewed in January, 1949; the patient had then complained of aching pain in the right lower lumbar region of several weeks' duration, as well as of pain in the right knee and the right thigh for seven years, which was thought to be due to an injury whilst on service with the Royal Australian Air Force. The thigh was enlarged with anterior bowing of the femur and limitation of extension at the knee joint and of rotation at the hip joint. He was tender about and below the right sacro-iliac region. Dr. Walpole demonstrated from the skiagrams numerous areas of decalcification and altered bone formation throughout the hip joint and femur. The enlargement of the upper portion of the femoral shaft was fusiform with gross thickening of the cortical bone and diminution of the marrow cavity. Early bone changes in the skull were also present. Dr. Walpole said that he had failed to find any evidence of carcinoma of the thyreoid or prostatic glands, that the serum had not given the Wassermann reaction, and that the blood acid phosphatase content was two units and the alkaline phosphatase content fifteen units compared with normal blood phosphatase levels (King Armstrong) of one and a half to four units. A sample of bone from the outer table of the ilium was removed for examination and was found to be normal. Dr. Walpole said that as he was able to exclude secondary carcinoma and specific osteitis, the diagnosis of Paget's disease of bone was made; treatment with calcium and vitamin *D* had resulted in slight general improvement. The disease process was advancing and he knew of no other treatment which was likely to be helpful.

DR. DOUGLAS THOMAS said that he agreed with the diagnosis and did not know of any effective treatment; he mentioned that the risk of sarcoma was recognized in the site of the lesion.

DR. J. E. SEWELL said that deep irradiation therapy might offer some hope; he knew of a case in which the pain had been eased thereby.

DR. MICHAEL KELLY said that he could recall a case that had lasted eight to ten years from the time of a pathological fracture, but he had not any suggestions to offer for promising treatment.

DR. ROBERT SOUTHBY asked Dr. Walpole for facts concerning the youngest age at which Paget's disease of bone was encountered. Dr. Walpole was unable to supply the information, but said that forty years was an early age for it to occur. Dr. Douglas Thomas stated that he had observed the condition in three patients for twenty years.

DR. F. J. KENNY said that he could quote a case in which calciferol, 50,000 units given twice daily, had relieved the pain.

Transthoracic Partial Gastrectomy.

DR. J. G. R. FELSTEAD showed two patients upon whom he had operated by the transthoracic route for partial removal of the stomach and œsophagus in the extirpation of carcinomata. He paid a tribute to the excellence of the anæsthesia produced by Dr. Walpole, who had used intravenously administered "Pentothal" and curare with cyclopropane; that had made the surgery possible. Dr. Felstead said that in each case the diagnosis had been obvious and the procedure standard, but he thought that the visitors might be interested to see the present state of the patients. Both felt well and could get about. Neither of them took unminced meat or solid food. Both had gained weight.

One man, sixty-five years of age, had undergone operation on October 11, 1948. He had had a history of increasing dysphagia and loss of weight. The œsophagoscope had been passed to its full length without meeting the growth. At operation the lowest inch of the œsophagus was found to be infiltrated and adherent to the diaphragm, and continuous with it was a large mass in the cardia, extending two-thirds of the way down the lesser curvature. It was not adherent to the pancreas. The liver felt normal. Glands were present in the greater omentum. Dr. Felstead had removed a little more than two-thirds of the stomach together with the lowest three inches of the œsophagus. He said that the pyloric end was anastomosed to the œsophagus above the growth. A Ryle tube was passed down through the nose, and the pleura was drained. Three pints of blood were given during the operation, which had lasted six and a half hours. The microscopic diagnosis was carcinoma infiltrating the muscle coats into the lymph channels; the tumour was partly anaplastic, partly clear-celled with mitoses. Dr. Felstead said that he had not had anxiety for more than ten minutes after the operation, as the patient had not been shocked or troubled by vomiting, distension or pain; the highest pulse rate was 96 per minute, and the highest temperature reached was 101·6° F. on the third day. The patient was discharged from hospital on the twenty-second day after operation.

The other patient shown by Dr. Felstead was a man, aged fifty-three years, who had undergone the operation on February 3, 1949, for carcinoma of the œsophagus. He had had a history, lasting two and a half months, of increasing dysphagia and loss of weight. By œsophagoscopy, an irregular constriction was seen low in the œsophagus; a portion snipped out was submitted to microscopic examination, and the report established the existence of carcinoma, anaplastic and epithelial in type. Dr. Felstead said that he had approached the growth by removing the eighth rib and one inch of the ninth rib. The growth involved the lowest two and a half inches of the œsophagus with considerable infiltration about the diaphragmatic opening and spreading over the cardia, large masses of glands near the spleen and three separate enlarged glands lying on the œsophagus above the growth. The œsophagus was freed almost to the aortic arch; four and a half inches of it, one-half of the stomach

and all the glands in the vicinity were removed; the pyloric end of the stomach was anastomosed to the proximal part of the œsophagus, and a Ryle tube was placed in position. The operating time was five hours and the patient received two pints of blood during the proceedings. Post-operatively there were no episodes of shock, vomiting, distension or cough; the pulse rate did not pass 80 per minute. Though ready to leave much sooner, the patient was discharged from the hospital on the thirty-fourth day after the operation.

DR. MICHAEL KELLY congratulated Dr. Felstead and Dr. Walpole on the two surgical feats and the anæsthetic administration, and made an inquiry concerning the prognosis, to which Dr. Felstead replied. He pointed out that operations were undertaken at a variety of stages in different cases and that a surgeon would need to have a very large series before the prognosis could be worked out in detail. He also referred to Dunlop's series, which had been published, and to the fact that the procedure was a standard one for the condition.

DR. DOUGLAS THOMAS also offered congratulations and commented on the pioneering of the transthoracic approach, which reduced the proportion of inoperable growths. With reference to the differential diagnosis of carcinoma involving the fundus, Dr. Thomas stated that no radiographic study of the stomach should be undertaken without the use of an antigravity procedure such as placing the patient in the Trendelenburg position; filling defects could be visualized by those procedures, which would be missed without them, and a negative report might be submitted, which would increase the diagnostic difficulty.

DR. ROBERT SOUTHBY said that the value of teamwork in private practice was admirably illustrated by Dr. Felstead's team at Horsham.

Traumatic Emboli of the Lower Extremities.

DR. BRIDGE showed a patient, a labourer, aged sixty-seven years, who had had an accident recently, the sequelæ of which were of considerable interest. The patient had not sought any medical attention for at least ten years and took pride in the fact that he was able to work like a young man. He had had three ribs broken in a crushing accident in 1933, but had recovered completely and had not had any dyspnœa of effort, intermittent claudication or muscle cramps. Dr. Bridge said that on the afternoon of March 2, 1949, the patient was caught and crushed between a truck and its trailer. The compressing force struck him just above the umbilicus, causing severe abdominal pain which made him fall to the ground. The pain had abated fairly quickly, but within two or three minutes he suffered intense burning pain in both feet. The pain in the feet was not relieved for thirty-six hours, though morphine was given several times. Soon after the accident the patient had noticed some blood-staining of the urine and he received emergency treatment. He was admitted to the Wimmera Base Hospital on the evening of March 4. His temperature was 100° F. His blood pressure was 160 millimetres of mercury (systolic) and 100 millimetres (diastolic); this was checked on the thighs and arms. The urine contained albumin, but no sugar; 20 red blood cells were seen per high-power field. The only other abnormal finding on routine clinical examination of the various systems was evidence of arterial hardening of the brachial, radial and retinal vessels. No bruises were found on the abdominal wall and no tenderness was elicited even on deep palpation. Both feet were cold and white, except where purple patches were developing symmetrically, but on the fifth toe of the left foot gangrene was commencing. There was a line of demarcation between hot and cold surfaces situated about two inches above each ankle joint. The femoral and popliteal pulses were all strong and, though the anterior and posterior tibial vessels could be felt as hard cords, they were not pulsatile. High spinal anæsthesia was induced in the ward, and the patient was placed in bed with the legs flat and at room temperature. The blood pressure fell to 100 millimetres of mercury (systolic) and 50 millimetres (diastolic), but no other objective changes were detected at the time. On March 6, a course of tetraethylammonium chloride ("Etamon") was commenced. On March 7, it was realized that there was not any hope that the collateral vessels would bring fresh blood to the feet, and on that day Dr. Felstead performed left lumbar sympathectomy; using the extraperitoneal approach, he removed the second, third and fourth lumbar ganglia. Many calcareous plaques were felt in the aorta, but no deep bruising was found in the limited region exposed. The operation did not check the developing gangrene of the left foot, which kept pace with the ischæmic changes in the right foot. The left leg was amputated below the knee on March 28, and the right leg was removed similarly on April 4. Dr. Bridge said that Dr. Wolkenstein had made a careful dissection of the vessels after amputation. In the main the arterial tracks were patent and the vessel walls looked normal, but on each side the anterior tibial artery was obstructed by a short adherent thrombus two or three centimetres above the ankle joint, and at the proximal end of the clot on the right side was a small, hard, yellow plaque, one or two millimetres in diameter; but no plaque was found on the left side. Dr. Bridge postulated that the pathological process was liberation by the sudden severe blow over the aorta of a shower of atheromatous emboli. The same sized plaques must have lodged at the same moment at the same sites and set up similar gangrenous processes. He said that the sympathetic supply to the lower limbs was from the second, third and fourth lumbar segments and did not pass through the cœliac plexus, but mostly through the femoral nerves. Emboli tended to lodge where the popliteal arteries divided into anterior and posterior tibial arteries and, if that happened, gangrene at the level encountered would be expected.

DR. MICHAEL KELLY said that there was another possible explanation. The whole arterial tree might have gone into a state of spasm after the injury, and the spasm might have been more severe and have lasted longer in the smaller and more remote vessels. He was very interested in the symmetry of the lesions. Damage to the artery in one limb could set up reflex spasm in the corresponding artery of the other; that had been shown by arteriograms and experiments had been performed with wire ligatures on cats. The whole arterial tree could go into spasm after a blow on the abdominal aorta.

Correspondence.

CONTROL OF HYPERTHYREOIDISM BY PROPYL THIOURACIL: A CLINICAL INQUIRY.

SIR: The article by Dr. Kempson Maddox on "Control of Hyperthyreoidism by Propyl Thiouracil: A Clinical Inquiry" in THE MEDICAL JOURNAL OF AUSTRALIA, July 23, 1949, is of considerable interest and importance in view of the frequency of this ailment in the eastern States of Australia. His critical analysis is to be commended as it entails close scrutiny of patients and time-consuming evaluation of records, which I fear not many among us will undertake.

It is only a little over six years since the "thio" drugs were introduced, and in the early days we did not quite know how to handle them, so that the methods and statistics published up to the end of 1946 (having indicated the pitfalls) should now be discarded and attention given to the fuller understanding of the subject in general and methods of treatment now available.

Dr. Maddox in his summary, paragraph 4, states: "Propyl thiouracil, with three times the therapeutic potency and ten times the safety of thiouracil or methyl thiouracil, should replace these drugs in the routine management of hyperthyreoidism." This statement is made despite the fact that with an increasing experience of its use his treatment dosage has been stepped up from 50-100 milligrammes *per diem* to 200-300 milligrammes and the maintenance dosage from 50-100 milligrammes or more *per diem*, that is, practically the same dosage that I advocate with methyl thiouracil. He thus comes into line with most workers in the United States of America, who also find that with the increased dosage necessary to obtain satisfactory clinical results there is a corresponding increase in toxic manifestations. Dr. Maddox states "the toxic effects are the same as occur with other members of the thiourea series", but does not give his percentage. Also eight patients out of the thirty-four treated by him had a toxic rash, eight patients showed leucopenia and six others a granulocytopenia—rather high figures for a small series. He states that in over 2000 patients treated to April, 1947, in the United States of America only five cases of agranulocytosis have been reported, that is, in the period of the smaller dosage, but since then many more cases are to be noted, and Bartels in his series of 672 cases with three of agranulocytosis also had eleven patients with severe leucopenia.

The use of methyl thiouracil has been neglected overseas, except in Scandinavia and England, until the last year or two, but a number of reports are being published of its use, and George Crile, junior, in his book "Practical Aspects of Thyroid Disease" just published states: "Methyl thiouracil given in smaller doses of 200-300 mgm. daily has not as yet proved toxic." Also: "Its action seems to be more prompt and more complete than that of propyl thiouracil, and to date the only toxic effect observed in a series of seventy

cases studied by Dr. E. Perry McCullagh at the Cleveland Clinic has been a mild dermatitis in one case." My own experience with methyl thiouracil has been eminently satisfactory, and with increasing experience any form of toxic reaction is becoming less common by adhering to the maxim that the smallest dose to secure a clinical effect is the safest dose. I am sure, too, that correctly balanced adjuvant therapy plays a big part.

E. P. McCullagh and W. T. Sirridge, reporting on 100 patients treated with methyl thiouracil (*Journal of Clinical Endocrinology*, December, 1948), noted as the only toxic manifestations four with mild rashes and one with leucopenia, but this patient had a history of previous blood dyscrasia. They regard methyl thiouracil as "somewhat more effective" than the propyl compound. In the same journal D. A. McGinty and others in an article "Excretion Studies on Thiouracil and its Derivatives in Man" show that methyl thiouracil reaches a peak in the blood plasma one and a half hours after ingestion and has a slow decline, whereas propyl thiouracil takes three and a half hours to reach its peak at a lower level and has a very rapid decline. They also state that 40% of thiouracil and of methyl thiouracil is excreted in the urine in twenty-four hours, but only 10% of propyl thiouracil. They conclude that propyl thiouracil is partially conjugated and thus inactivated on absorption and this accounts for its slower action. Added to these observations is the work of Stanley and Astwood on the uptake of radioactive iodine by the thyreoid gland and the effect of various "thio" compounds, in which they found methyl thiouracil to be twice as effective as thiouracil while propyl thiouracil was 25% less effective than thiouracil.

In his original work on the potency of various compounds for controlling thyreoid activity in rats, Astwood found propyl thiouracil ten times more effective than thiouracil, but when they were applied to man this claim was not substantiated and now we have the reverse in the case of mercapto-imidazole, which in rats had one to five times the potency of thiouracil, but is ten times more potent in man.

That there is a case for the use of methyl thiouracil rather than propyl thiouracil would seem to be established by the experimental work mentioned, by the results obtained in a large series of cases already published by me, and the low toxicity in correct dosage reported by me and by other observers.

As regards the question of thyreotoxicosis in pregnancy, I have now eighteen patients who have been carried through pregnancy safely with methyl thiouracil and with normal babies, but the drug is stopped during the last two months and iodine given in small doses to allow for the normal rise in basal metabolic rate in this period. As Dr. Maddox "would hesitate to use propyl thiouracil" with a severe thyreotoxicosis in pregnancy he should try methyl thiouracil. He states that operation is preferable with a thyreocardiac, but unless the cause is an adenomatous toxic thyreoid, I do not recommend operation, as patients remain well with normal cardiac rhythm under correct management.

In conclusion, I would like to quote from two personal communications: (i) from E. B. Astwood, April 2, 1947: "I feel that your observations are the most important contribution to this field for some time and I feel they have taught us just how we should manage thyreotoxicosis with an antithyroid drug", and (ii) from George Crile, junior, April 29, 1947: "We have used methyl thiouracil in about 30 cases to date, but it appears the drug is relatively more effective than propyl thiouracil has been in our hands. I think your results are the best that I have heard to date."

Yours, etc.,

225 Macquarie Street,
Sydney,
July 25, 1949.

HUGH R. G. POATE.

BLOOD ALCOHOL CONTENT: SOME ASPECTS OF ITS POST-MORTEM USES.

SIR: It was with much interest that we read the article by K. M. Bowden and N. E. W. McCallum entitled "Blood Alcohol Content: Some Aspects of its Post-Mortem Use" in THE MEDICAL JOURNAL OF AUSTRALIA of July 16, 1949, on page 76. We regard this paper as a most valuable contribution to the literature on the subject.

We feel, however, that we cannot accept without comment the authors' statement that "blood taken from the heart after death for purposes of blood alcohol estimations is reliable for a quantitative estimation only if taken almost

DISEASES NOTIFIABLE IN EACH STATE AND TERRITORY OF AUSTRALIA AND NOTIFICATIONS FOR THE WEEK ENDED JULY 16, 1949.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	1	2	..	2	..	..	..	5
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	1	1	2	..	..	..	..	..	4
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(a)	*	*	1	*	*	*	*	*	1
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	2	..	..	..	..	..	2
Diphtheria	17	11	4	..	3	..	..	..	35
Dysentery(b)	*	1	..	..	1	..	..	..	2
Encephalitis Lethargica	1	..	..	..	..	..	..	..	1
Erysipelas	*	*	*	1	*	*	..	..	1
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	1	*	*	..	2	*	..	3
Influenza	*	*	*	..	*	*	..	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(c)	*	(c)	1(c)	(c)	(c)	(c)	(c)	(c)	1(c)
Measles	*	*	*	117	*	*	..	..	117
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	20	..	7	2	..	..	..	30
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	2	..	..	..	..	..	2
Rubella	*	*	*	*	*	*	..	..	..
Scarlet Fever	27	13	9	10	2	4	..	..	65
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	1	*	*	*	*	*	1
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(d)	19	15	4	2	7	4	..	..	51
Typhoid Fever(e)	..	..	..	..	1	..	..	..	1
Typhus (Endemic)(f)	..	..	..	..	2	..	..	..	2
Undulant Fever	..	..	..	..	1	..	..	..	1
Weil's Disease(g)	*	*	..	*	*	*	*	*	..
Whooping Cough	*	*	*	57	*	*	..	..	57
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 36, 1944-1945.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from Northern Territory.
* Not notifiable.
(a) Includes "Mossman" and "Sarina" fevers. (b) Includes amœbic and bacillary. (c) Statistics inexact with varying practice with regard to relapses in Service cases infected overseas. (d) Includes all forms except in New South Wales and Northern Territory, where only pulmonary tuberculosis is notifiable. (e) Includes enteric fever and paratyphoid fevers. (f) Cases reported are all of the mild type known as Brill's disease or endemic typhus (including scrub and urban types). (g) Includes leptospiroses, Weil's and para-Weil's disease.

immediately after death". Recently it has been our practice to have alcohol estimations performed on blood taken at autopsy both from the heart and femoral vein and our findings in twelve consecutive cases are set out in the accompanying table.

Case.	Hours Since Death.	Alcohol Concentration in Milligrammes per 100 Millilitres.		
		Femoral Vein.	Heart.	Urine.
1	35	30	30	—
2	40	90	90	150
3	13	120	120	170
4	33	110	110	240
5	33	80	80	130
6	18	180	180	150
7	43	50	50	—
8	36	120	120	230
9	24	300	300	—
10	15	70	70	120
11	10	180	180	400
12	51	170	170	270

It will be seen that in this series, identical results were obtained for the alcohol concentration from heart blood and peripheral blood up to forty-three hours after death. This indicates that when death occurred, absorption of alcohol from the stomach had proceeded to a point where equilibrium had been established. We believe that this state of affairs is usual in cases coming to autopsy and that the circumstance simulated by the authors' experiment in which death occurs within a few minutes of drinking a large quantity of alcohol (six to ten ounces of whisky) is rare.

While we would agree that it is desirable at autopsy to collect blood from the peripheral vein for alcohol estimation, we nevertheless feel that in the past when reliance has been placed on estimations performed on heart blood, very few erroneous conclusions have been drawn due to falsely high heart blood alcohol concentrations.

Yours, etc.,
J. I. TONGE.
J. O'REILLY.

Laboratory of Micro-Biology and Pathology,
Department of Health and Home Affairs,
William Street,
Brisbane.
July 21, 1949.

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned has been registered, pursuant to the provisions of *The Medical Acts, 1939 to 1948*, of Queensland, as a duly qualified medical practitioner:

White, Linus, M.B. 1946 (Univ. Sydney), c.o. Hospitals Board, Townsville.

The following additional qualification has been registered:

Howell, David John, Repatriation General Hospital, Greenslopes, Brisbane, D.T.M. and H. (Univ. Sydney), 1948.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1939, of New South Wales, as duly qualified medical practitioners:

Bauer, Franz, M.B., B.S., 1942 (Univ. Adelaide), Repatriation Hospital, Concord.

Davies, William Robert, M.B., B.S., 1948 (Univ. Sydney), Royal Perth Hospital, Perth.

Ettelson, Eric Mendel, M.B., B.S., 1920 (Univ. Melbourne), c.o. National Bank of Australasia, Balaclava, Victoria.

Francis, Shirley Evelyn Amy Lorraine, M.B., B.S., 1945 (Univ. Melbourne), 9 Macleay Street, Bondi Beach.

Haughton, Samuel Francis Hewitt, M.B., B.Ch., 1940 (Univ. Dublin), Flinders Naval Depot, Melbourne.

Hewer, George Frederick, M.B., Ch.M., 1919 (Univ. Sydney), Narromine.

Morgan, Bertram Charles, M.B., B.S., 1947 (Univ. London), R.A.N. Air Station, Nowra.

Paull, Torrance Arnold, M.B., B.S., 1947 (Univ. Adelaide), 372 Chloride Street, Broken Hill.

The following additional qualifications have been registered:

Hertzberg, Reuben, 9 Butler's Road, Hurstville (M.B., 1939, Univ. Sydney, Dip.Ophth., Melbourne, 1946), F.R.A.C.S., 1948.

Raftos, John, 8 Duntroon Avenue, Roseville (M.B., B.S., 1945, Univ. Sydney), M.R.A.C.P., 1949.

Speirs, Robert Bradley, 85 Archbold Road, Lindfield (M.B., B.S., 1938, Univ. Sydney), D.A., 1949.

Diary for the Month.

AUG. 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

AUG. 11.—Victorian Branch, B.M.A.: Organization Subcommittee.

AUG. 12.—Queensland Branch, B.M.A.: Council Meeting.

AUG. 15.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135 Macquarie Street, Sydney): Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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